Immunologic and antiserum compositions useful as reagents in heragglutination inhibition tests for pregnancy were prepared. Stabilized hCG sensitized red blood cells were suspended in a lyophilization medium which contained a suitable carbohydrate diluent, buffer, sodium chloride, normal. . .

US PAT NO: 4,315,908 [IMAGE AVAILABLE] L1: 8 of 13

DETDESC:

DETD(12)

The . . . sampling and sixty days after sampling and as can be seen the results are practically the same which proves the stability of HCG in the performance of the method according to the invention.

DETDESC:

DETD(14)

TABLE 1

Stability of urinary HCG on the stick. (a) (N = 530)

	day 0	day 1	day 60 at room temperature

. . .

```
=> s l1 and trehalose
          1039 TREHALOSE
L2           0 L1 AND TREHALOSE

=> s l1 and glutamate
          2727 GLUTAMATE
L3           0 L1 AND GLUTAMATE

=>  s l1 and isicitrate
             0 ISICITRATE
L4           0 L1 AND ISICITRATE

=> s l1 and isocitrate
           103 ISOCITRATE
L5           0 L1 AND ISOCITRATE

=> s l1 and tartrate
          8548 TARTRATE
L6           0 L1 AND TARTRATE

=> LOG Y
U.S. Patent & Trademark Office LOGOFF AT 11:26:32 ON 31 JAN 92
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PROG:

-1-
AN - 84-071338/12
XRAM- C84-030601
TI - Stabilising beta-interferon having no sugar chain - by adding poly:ol, e.g. ethylene glycol, glycerine or sugar, esp. oligo saccharide
DC - B04 D16
PA - (TORA) TORAY IND INC
NP - 1
PN - J59025333-A 84.02.09 (8412) (JP)
PR - 82.08.03 82JP-135422
AP - 82.08.03 82JP-135422
IC - A61K-045/02 C07G-007/00 C12N-015/00 C12P-021/00
AB - (J59025333)
Stabilisation of beta-interferon having no sugar chain (G-IFN-beta) comprises adding a polyol (specifically glycerine or sucrose in amt. 5% or more) to G-IFN-beta. G-IFN-beta is produced by microorganisms generated by recombinant DNA techniques.

For example, E. coli HB101 contg. plasmid pLG117R contg. human IFN-beta was pre-incubated on LB medium. 1 l was inoculated on LB medium at 2% and incubated at 30 deg.C with shaking until OD(660) reached 0.6. The organisms were washed with 50 mM Tris buffer (pH 8.0) contg. 25% sucrose, collected by centrifugation, and dispersed in 20 ml 20 mM EDTA-50 mM Tris-buffer (pH 8.0), to which 2.0 mg/ml lysozyme was added. The mixt. was stood at 0 deg.C for 30 mins., lytically reacted by lyophilisation, and centrifuged at 15,000 rpm for 60 mins., to give a supernatant of G-IFN-beta (1100U/ml). Polyol includes glycerine, ethylene glycol and sugar (pref. oligosaccharide), which may be added to the supernatant of G-IFN-beta in amt. 5% or more, pref. 10-30%.

Human fibroblast interferon-beta (F-IFN-beta) is glycoprotein of mol. wt. 23000 + or -2000, consisting of protein portion (MW 20,000) and sugar portion (MW 3000). G-IFN-beta (MW 20,000) is less stable than F-IFN-beta and inactivated at 15 deg.C, which is lower than that of F-IFN-beta. (4pp Dwg.No.0/0)

SS 4 /C?
USER:
FILE USCLASS

PROG:
ELAPSED TIME ON WPAT: 0.07 HRS.
YOU ARE NOW CONNECTED TO THE USCLASS DATABASE.

```
=> stabili?(5a)(hcg or gonadotropin?)
        287590 STABILI?
           669 H"G
           948 GONADOTROPIN?
L1          13 STABILI?(5A)(HCG OR GONADOTROPIN?)

=> d kwic

US PAT NO:      4,966,800 [IMAGE AVAILABLE]                    L1: 1 of 13

DETDESC:

DETD(28)

 From . . . their molecular weight ranges of about 34,000 to 38,000
and about 70,000 to 85,000, respectively, their specific binding
capability for  hCG  and their  stability  under the various
```

conditions or treatment heretofore described. In turn, these basic units appear to be linked through covalent disulfide. . .

=> d 1-13

1. 4,966,888, Oct. 30, 1990, hCG-hLH receptor and hCG-hLH receptor-hCG complex as antigens, antibodies thereto and contraceptive vaccine; Brij B. Saxena, et al., 514/2; 424/88; 435/7.1, 70.3; 514/8, 12; 530/350, 398, 399 [IMAGE AVAILABLE]

2. 4,880,914, Nov. 14, 1989, Assay for qualitatively and/or quantitatively measuring hLH or hCG in body fluids and reagents therefor; Brij B. Saxena, et al., 530/395; 424/88; 514/8; 530/397, 398, 412, 413 [IMAGE AVAILABLE]

3. 4,727,024, Feb. 23, 1988, Binding assays involving formation and detection of light scattering crystals; Martin Kaocher, et al., 435/7.4, 7.8, 810; 436/36, 501, 518, 525, 536, 805, 808, 809

4. 4,550,649, Dec. 24, 1985, Assaying for hLH or hCG with immobilized hormone receptors; Brij B. Saxena, et al., 435/7.21, 7.8, 7.92, 181, 188, 810, 961, 963, 964, 975; 436/501, 527, 805, 810, 817, 818; 530/313, 397, 398, 399, 812

5. 4,383,036, May 10, 1983, Process for the production of human chorionic gonadotropin; Kaname Suginoto, 435/70.2, 70.4, 172.2; 530/398; 935/71, 99, 100, 106, 107, 109

6. 4,351,158, Sep. 28, 1982, Method of producing multicomponent lyophilized product; Arthur Hurwitz, et al., 62/60; 34/5; 62/66, 74; 141/9, 11, 100

7. 4,320,111, Mar. 16, 1982, Immunologic compositions methods of preparation and use; Michael R. Hirsch, et al., 435/7.25; 424/3, 11, 533; 435/4, 961; 436/521; 514/6; 530/395, 397, 398, 399, 405, 406, 410, 806, 810, 829

8. 4,315,908, Feb. 16, 1982, Method of determining human chorionic gonadotropin (HCG) in the urine; Tamar Zer, et al., 424/1.1; 422/61; 436/510, 532 [IMAGE AVAILABLE]

9. 4,295,280, Oct. 20, 1981, Method of obtaining a lyophilized product; John Krupey, 34/5; 62/60

10. 4,218,335, Aug. 19, 1980, Stabilizer for an immunochemical measuring reagent; Ei Mochida, et al., 436/518; 435/188, 963; 436/520, 533, 534, 543, 814, 817, 818, 826; 530/371, 401, 841

11. 4,208,187, Jun. 17, 1980, Diagnostic test; Morris L. Givner, 436/521; 210/645; 422/59, 69, 101; 436/543, 547, 807, 808, 814, 817, 818, 825, 826

12. 4,138,214, Feb. 6, 1979, Diagnostic test utilizing human chorionic gonadotropin; Morris L. Givner, 436/521, 520, 807, 814, 818, 825

13. 3,991,175, Nov. 9, 1976, Composition and method for determination of pregnancy; Lea Grundman, 436/521; 424/3, 533; 436/547, 814, 818, 826

=> d 6 8 kwic

US PAT NO: 4,351,158 L1: 6 of 13

DETDESC:

DETD(6)

10. 4,806,524, Feb. 21, 1989, Stable erythropoietin preparation and process for formulating the same; Tsutomu Kawaguchi, et al., 514/8, 970; 530/395

11. 4,803,073, Feb. 7, 1989, Process for the pasteurization of plasma proteins and plasma protein fractions; Walter Doleschel, et al., 424/530; 435/236, 238; 514/2, 21, 802; 530/380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 427, 830

12. 4,748,040, May 31, 1988, Process for the manufacture of a frothy drink composition; Theo W. Kuypers, 426/569, 470, 570, 580, 583, 584, 585, 590, 593, 594, 613

13. 4,748,034, May 31, 1988, Preparing a heat stable aqueous solution of whey proteins; Olivier de Rham, 426/330.2, 491, 583

14. 4,746,527, May 24, 1988, Drink composition; Theo W. Kuypers, 426/569, 470, 570, 580, 583, 584, 585, 590, 593, 594, 613

15. 4,727,059, Feb. 23, 1988, Fibronectin solution suitable for use in humans and process for its preparation; Bernd Binder, et al., 514/8, 21; 530/380, 386, 392, 395

16. 4,691,011, Sep. 1, 1987, Water-dispersible hydrophilic milk protein product; Kaoru Inagami, et al., 530/832, 833

17. 4,689,238, Aug. 25, 1987, Composite food product; Elinor Hitchner, 426/571, 89, 93, 564, 568, 576

18. 4,623,717, Nov. 18, 1986, Pasteurized therapeutically active protein compositions; Peter M. Fernandes, et al., 530/380; 435/188; 514/8, 21; 530/381, 382, 383, 386, 393, 830

19. 4,500,553, Feb. 19, 1985, Method of producing a frozen dual-textured confection; Louis G. Liggett, et al., 261/1; 426/134, 249, 565, 576

20. 4,482,575, Nov. 13, 1984, Aerated oil-based cheese mixture; Dale F. Olds, 426/582, 585, 613

21. 4,470,968, Sep. 11, 1984, Pasteurized therapeutically active blood coagulation factor concentrates; Gautam Mitra, et al., 530/384; 514/8

22. 4,440,679, Apr. 3, 1984, Pasteurized therapeutically active protein compositions; Peter M. Fernandes, et al., 530/363; 424/85.8, 530; 435/188; 514/21; 530/380, 381, 382, 383, 386, 387, 389, 392, 393, 394, 395, 399, 410, 414, 427

23. 4,416,784, Nov. 22, 1983, Filling composition for use in liquid chromatography; Masaaki Nakao, et al., 210/635; 422/70

24. 4,379,085, Apr. 5, 1983, Heat stabilization of plasma proteins; Craigenne A. Williams, et al., 530/381, 363, 380, 384, 393, 830

25. 4,362,756, Dec. 7, 1982, Brown sugar sweetened condensed milk and process for preparation thereof; Alexander W. Williams, 426/587, 658

26. 4,309,417, Jan. 5, 1982, Protein fortified isotonic beverages; Lorna C. Staples, 424/601, 722; 426/583, 590, 648; 514/21

27. 4,308,294, Dec. 29, 1981, Oil replacement composition; Joseph M. Rispoli, et al., 426/564, 567, 575, 576, 577, 578, 603, 613, 656, 657

28. 4,296,134, Oct. 20, 1981, Liquid egg blend; Wayne A. Boldt, 426/250, 614

29. 4,272,533, Jun. 9, 1981, Fractionating citrate-stabilized plasma; Ronald Kotitschke, et al., 530/382, 380, 383, 384, 393, 830

30. 4,260,636, Apr. 7, 1981, Preparation of a fermented milk drink; Mutsuo Yasumatsu, et al., 426/34, 43, 522, 584, 590

31. 4,194,019, Mar. 18, 1980, Preparation of an acidified milk beverage; Mutsuo Yasumatsu, et al., 426/580, 522, 590

32. 4,092,438, May 30, 1978, Non-dairy coffee whitener containing acetate salt; George F. Tonner, 426/601, 613, 656, 658

33. 4,089,983, May 16, 1978, Color-stabilized semi-moist food and process; Larry L. Hood, 426/250, 263, 264, 265, 540, 647, 657, 805

34. 4,038,140, Jul. 26, 1977, Process for binding biologically active proteins; Dieter Jaworek, et al., 435/178, 180; 525/54.1, 54.31; 527/201, 202, 203, 313

35. 4,011,346, Mar. 8, 1977, Process for the production of a formed high moisture pet food product; Thomas J. Ernst, 426/104, 332, 335, 532, 646, 656, 802, 805

36. 3,935,323, Jan. 27, 1976, Process for improving whipping properties of aqueous protein solutions; Joseph V. Feminella, et al., 426/564, 572, 583

37. 3,663,235, May 16, 1972, PROCESS OF PREPARING MARGARINE CONTAINING DIACYGLYCEROPHATIDE; Hans-Udo Menz, et al., 426/604; 252/309, 312, 356; 260/403 [IMAGE AVAILABLE]

38. 3,624,198, Nov. 30, 1971, RODENTICIDE BAIT; Howard L. Arbaugh, 424/410, 474, 604

=> d 12 8 kwic

US PAT NO: 4,816,568 L2: 8 of 38

CLAIMS:

CLMS(11)

11. . . . promotion in animals comprising administering to the animal an effective amount of a stabilized growth promoting formulation comprising a growth hormone with a stabilizing amount of a stabilizer selected from one or more of the following:
(a) an amino acid selected from the group consisting of glycine, sarcosine, lysine or salts thereof, serine, arginine or salts thereof, betaine, N,N-dimethylglycine, aspartic acid or salts thereof, glutamic acid or salts thereof,
(b) a polymer of an amino acid having a charged side group at physiological pH; and
(c) a choline derivative selected from the group consisting of choline chloride, choline dihydrogen citrate, choline bitartrate, choline bicarbonate, tricholine citrate, choline ascorbate, choline borate, choline gluconate, choline phosphate, di(choline)sulfate and dicholine mucate.

CLAIMS:

CLMS(21)

21. A stabilized growth promoting formulation comprising a growth hormone and a stabilizing amount of a stablizer selected from one or more of the following:
(a) an amino acid selected from the group consisting of glycine,

sarcosine, lysine or salts thereof, serine, creatine or salts thereof, betaine, N,N-dimethylglycine, aspartic acid or salts thereof, glutamic acid or salts thereof,

(b) a polymer of an amino acid having a charged side group at physiological pH; and

(c) a choline derivative selected from the group consisting of choline chloride, choline dihydrogen citrate, choline bitartrate, choline bicarbonate, tricholine citrate, choline ascorbate, choline borate, choline gluconate, choline phosphate, di(choline)sulfate and dicholine mucate.

=> LOG Y
U.S. Patent & Trademark Office LOGOFF AT 07:44:55 ON 27 JUN 91

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=> s gonadotropin?
L1          578 GONADOTROPIN?

=> s l1 and trehalose
          1039 TREHALOSE
L2           7 L1 AND TREHALOSE

=> d kwic

US PAT NO:      4,966,856 [IMAGE AVAILABLE]              L2: 1 of 7

DETDESC:

DETD(4)
  .  .  .
and
                    complementary factor.
(Peptide hormones)
Adrenocorticotropin (ACTH),
                    methionine- and leucine-
                    enkephalin,
thyroxine, and      triiodothyronine.
(Protein hormones)
Chorionic   gonadotropin  ,
                    chorionic tyrotropin,
glucagon,           insulin,
nerve growth factor,
                    parathyroid hormone,
placental lactogens,
                    prolactin,
proinsulin, and     relaxin
(Tissue hormones).  .  .

DETDESC:

DETD(275)

 Concrete examples of such materials include gelatin, gelatin-decomposed
materials, albumin, BSA, cyclodextrans, non-reducing sugars (sucrose,
  trehalose  ), polyethylene glycol, amino acids, various ions, sodium
azide, and the like. These preservatives are desirable to be present in
the.  .  .

=> d 1-7

1.  4,966,856, Oct. 30, 1990, Analytical element and the analytical
method using the element; Tsukasa Ito, et al., 436/170; 422/56, 57, 58;
435/4, 7.8, 7.93, 28, 805, 970; 436/172, 804, 805 [IMAGE AVAILABLE]

2.  4,931,385, Jun. 5, 1990, Enzyme immunoassays and immunologic
reagents; Elliott Block, et al., 435/7.94, 28, 188, 805, 810, 975;
436/510, 808, 810, 814, 816, 826 [IMAGE AVAILABLE]

3.  4,868,105, Sep. 19, 1989, Analytical element and method for
determining a component in a test sample; Tsukasa Ito, et al., 435/7.7;
422/56, 57; 435/7.5, 7.71, 7.72, 7.8, 7.92, 7.94, 805, 968; 436/501, 510,
524, 527, 528, 529, 530, 531, 800, 810, 827, 828 [IMAGE AVAILABLE]
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4. 4,824,938, Apr. 25, 1989, Water-soluble dry solid containing proteinaceous bioactive substance; Shunsaku Koyama, et al., 530/351; 424/85.1, 94.1, 94.2, 94.3; 435/102, 108; 514/2, 3, 8, 23; 530/350, 399; 536/1.1

5. 4,517,290, May 14, 1985, Method for enzyme immunoassay and peptide-enzyme conjugate and antibody therefor; Susumu Iwasa, et al., 435/7.93; 424/88; 435/7.92, 183, 810, 961, 963, 967, 971, 975; 436/510, 547, 814; 530/324, 325, 326, 327, 328, 345, 387, 806; 930/10, DIG.705, DIG.811

6. 4,496,650, Jan. 29, 1985, Method for enzyme immunoassay and production of antibody; Keiichi Kondo, et al., 435/7.94, 975; 436/510, 512, 531, 543, 544, 545, 546, 547, 800, 804, 808, 813, 814, 819; 930/110, 200, DIG.705, DIG.821

7. 4,410,512, Oct. 18, 1983, Method for preparing a purified extraction residue fraction and its use in stimulating the immune response; Virginia Livingston-Wheeler, et al., 424/92, 88; 435/822

=> d 4 kwic

US PAT NO: 4,824,938 L2: 4 of 7

SUMMARY:

DSUM(13)

In . . . surface active agents, and Japan Patent Kokai No. 59,625/84 proposes D-glucose, D-galactose, D-xylose, D-glucuronic acid, dextran, hydroxyethyl starch, and, preferably, trehalose . The stabilization effects attained with these stabilizers have proved insufficient. In addition, trehalose is relatively expensive. Thus, these stabilizers have not been in practical use.

SUMMARY:

3SUM(16)

The . . . factor, transfer factor, T cell growth factor, and colony stimulating factor; and peptide hormones, such as insulin, GH, prolactin, chorionic gonadotropin , EPO, follicle-stimulating hormone, luteinizing hormone, EGF, adrenocorticotropic hormone, placental lactogen, TSH, and parathyroid hormone, which have a molecular weight within. . .

=> s l2 and dicarboxylic
27692 DICARBOXYLIC
L3 0 L2 AND DICARBOXYLIC

=> s l2 and (citrate or tartrate or tartarate)
19796 CITRATE
8048 TARTRATE
839 TARTARATE
L4 2 L2 AND (CITRATE OR TARTRATE OR TARTARATE)

=> d 1-2

1. 4,931,385, Jun. 5, 1990, Enzyme immunoassays and immunologic reagents; Elliott Block, et al., 435/7.94, 28, 188, 805, 810, 975; 436/510, 808, 810, 814, 818, 826 [IMAGE AVAILABLE]

2. 4,517,290, May 14, 1985, Method for enzyme immunoassay and peptide-enzyme conjugate and antibody therefor; Susumu Iwasa, et al., 435/7.93; 424/88; 435/7.92, 183, 810, 961, 963, 967, 971, 975; 436/510, 547, 814; 530/324, 325, 326, 327, 328, 345, 387, 806; 930/10, DIG.705,

=> d kwic

US PAT NO: 4,931,385 [IMAGE AVAILABLE] L4: 1 of 2

SUMMARY:

BSUM(4)

There . . . home diagnostic immunoassay kits which may be readily used, for example, for the detection of antigens such as human chorionic gonadotropin hormone (hCG, antigen) which is present in the urine of pregnant women. In order for a diagnostic immunoassay kit to. . .

SUMMARY:

BSUM(24)

In . . . antibody sandwich technique has been found well suited to the diagnosis of a variety of antigens such as human chorionic gonadotropin hormone (hCG), gonococcus bacteria (GC), and human leutinizing hormone (hLH).

SUMMARY:

BSUM(25)

In . . . enhancing agent to enhance formation of an immune complex, a surfactant and sugar selected from an oligosaccharide, preferably dextrins and trehalose and the solution subsequently lyophilized, the conjugate will maintain reactivity binding specificity and avidity even if subjected to hot and/or. . .

SUMMARY:

BSUM(28)

Surprisingly, applicant has found that inclusion of suitable oligosaccharides preferably containing disaccharides (but not sucrose) and more preferably containing dextrin or trehalose sugars have been determined to be important components in the lyophilization mixture. The criticality associated with the selection of specific. . . However, it is not fully understood why so distinctly favorable results have been obtained with the use of dextrins and trehalose sugars. These species may have physiochemical properties which impart markedly greater stability and homogeneity to the lyophilized mixture.

SUMMARY:

BSUM(31)

Prior . . . exposed to both a surface active component and polyethylene glycol in the lyophilization solution provided specific sugars, e.g., dextrins or trehalose sugars are included as additives into the lyophilization solution containing conjugate.

SUMMARY:

BSUM(33)

The . . . of sugars is water soluble. Examples of suitable monosaccharides are glucose and fructose. Examples of suitable disaccharides are sucrose, maltose, trehalose and lactose and a suitable saccharide mixture is dextrin. It has been determined that the blocking agent to be employed. . .

observed that a additive including polyethylene glycol (PEG) facilitates immunologic reactions of antigen,. . .

DETDESC:

DETD(3)

The following protocol was carried out as a colorimetric antibody sandwich ELISA for human chorionic _gonadotropin_ hormone (hCG). The procedure involved coating a solid support with a first antibody, adding an antigen sample and simultaneously supplying. . .

DETDESC:

DETD(5)

The . . . of different sugars is water soluble. Typical examples of suitable monosaccharides are glucose and fructose. Typical disaccharides are sucrose, maltose, _trehalose_ and lactose; and typical suitable saccharide mixture is dextrin. Instead of bovine serum albumin (BSA) the
=>
=> LOG Y
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SUMMARY:

BSUM(37)

Although . . . antibodies, they have been found of particular utility in home diagnostic kits for detection of antigens such as human chorionic _gonadotropin_ hormone (hCG), present in the urine of pregnant women; Neisseria gonorrhea, the bacteria causing gonorrhea, also called gonococcus (GC); and. . .

SUMMARY:

BSUM(41)

It . . . a binding enhancing agent to enhance formation of an immune complex, a surfactant and sugar preferably selected from dextrins and _trehalose_ and the solution subsequently lyophilized the conjugate will maintain reactivity binding specificity and avidity even if subjected to hot and/or. . .

SUMMARY:

BSUM(43)

Surprisingly applicant has found that inclusion of suitable oligosaccharides preferably containing disaccharides (but not sucrose) and, more preferably containing dextrin or _trehalose_ sugars are important components in the lyophilization mixture. The criticality associated with the selection of specific classes of sugars has. . . However, it is not fully understood why so distinctly favorable results have been obtained with the use of dextrins and _trehalose_ sugars. Dextrin is a mixture of glucose, the disaccharide maltose, and higher molecular weight saccharides. _Trehalose_ is a disaccharide containing two D-glucose residues. Dextrin and _trehalose_ appear to have physicochemical properties which impart markedly greater stability and homogeneity to the lyophilized mixture.

SUMMARY:

BSUM(46)

Prior . . . component and the aforementioned binding enhancing agents, particularly polyethylene glycol, in the lyophilization solution provided specific sugars, e.g., dextrins or _trehalose_ sugars are included as additives into the lyophilization solution containing conjugate. The lyophilized product mixture of the present invention containing. . .

SUMMARY:

BSUM(51)

The . . . of sugars is water soluble. Examples of suitable monosaccharides are glucose and fructose. Examples of suitable disaccharides are sucrose, maltose, _trehalose_ and lactose and a suitable saccharide mixture is dextrin. It has been determined that the blocking agent to be employed. . .

SUMMARY:

BSUM(57)

The . . . by a buffer to provide a suitable medium for the simultaneous incubations of the invention. In testing for human chorionic _gonadotropin_ (hCG) and leutinizing hormone (hLH) applicants have

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PLEASE ENTER HOST PORT ID:x
LOGINID:s (protein# or hormone#)(3a)stabili?
          33669 PROTEIN#
           8245 HORMONE#
         274869 STABILI?
L1   859 (PROTEIN# OR HORMONE#)(3A)STABILI?

=> s l1 (p)(dicarboxylic or aspartate or aspartic or citric or citrate or glutam
ic or glutamate)
          26440 DICARBOXYLIC
           1005 ASPARTATE
           4590 ASPARTIC
          28632 CITRIC
          18730 CITRATE
           5887 GLUTAMIC
           2566 GLUTAMATE
L2   38 L1 (P)(DICARBOXYLIC OR ASPARTATE OR ASPARTIC OR CITRIC OR C
ITR
                 ATE OR GLUTAMIC OR GLUTAMATE)

=> d kwic

US PAT NO: 4,938,856 [IMAGE AVAILABLE]   L2: 1 of 38

SUMMARY:

BSUM(3)

 By . . . the acidity (increasing the pH), the taste of products can
be improved, the viscosity can be modified, the color and protein
 stability can be enhanced. Acids, such as citric , have been added
to some moderately acid fruits and vegetables to lower the pH to a value
below 4.5 permitting. . .

=> s l2 and (lyophil? or freeze dried or freeze drying)
          11245 LYOPHIL?
          21779 FREEZE
         192811 DRIED
           6005 FREEZE DRIED
                  (FREEZE(W)DRIED)
          21779 FREEZE
         136106 DRYING
           4862 FREEZE DRYING
                  (FREEZE(W)DRYING)
L3   14 L2 AND (LYOPHIL? OR FREEZE DRIED OR FREEZE DRYING)

=> d kwic

US PAT NO: 4,909,941 [IMAGE AVAILABLE]   L3: 1 of 14

SUMMARY:

BSUM(20)

It . . . is a carboxylic acid which is present in vivo in a biochemical pathway such as the glycolytic pathway or the citric acid cycle. Not only are these acids of a natural origin and thus suitable in pharmaceutical applications, but unexpectedly these acids allow stabilization of the native protein structure (so as to control the undesired interactions between the support phase and the solute) as well as allowing elution of the protein sample under milder chromatographic conditions. Because of the stabilization of protein structure (and thereby limiting the number of hydrophobic contacts with the reversed phase) a lower concentration of organic solvent or. . .

DETDESC:

DETD(31)

The . . . about 20% alcohol and subjected to ultrafiltration. By this technique the buffer components are removed. Subsequently, the albumin may be freeze dried to a colorless powder. Alternatively, the albumin solution can be adjusted to a desirable buffer composition for direct use.

=> d 1-14

1. 4,909,941, Mar. 20, 1990, High performance liquid chromatography mobile phase; Dick J. Poll, et al., 210/635, 542, 656; 530/305, 371, 399, 417 [IMAGE AVAILABLE]

2. 4,806,524, Feb. 21, 1989, Stable erythropoietin preparation and process for formulating the same; Tsutomu Kawaguchi, et al., 514/8, 970; 530/395

3. 4,803,073, Feb. 7, 1989, Process for the pasteurization of plasma proteins and plasma protein fractions; Walter Doleschel, et al., 424/530; 435/236, 238; 514/2, 21, 802; 530/380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 427, 830

4. 4,748,034, May 31, 1988, Preparing a heat stable aqueous solution of whey proteins; Olivier de Rham, 426/330.2, 491, 583

5. 4,691,011, Sep. 1, 1987, Water-dispersible hydrophilic milk protein product; Kaoru Inagami, et al., 530/832, 833

6. 4,623,717, Nov. 18, 1986, Pasteurized therapeutically active protein compositions; Peter M. Fernandes, et al., 530/380; 435/188; 514/8, 21; 530/381, 382, 383, 386, 393, 830

7. 4,470,968, Sep. 11, 1984, Pasteurized therapeutically active blood coagulation factor concentrates; Gautam Mitra, et al., 530/384; 514/8

8. 4,440,679, Apr. 3, 1984, Pasteurized therapeutically active protein compositions; Peter M. Fernandes, et al., 530/363; 424/85.8, 530; 435/188; 514/21; 530/380, 381, 382, 383, 386, 387, 389, 392, 393, 394. 395, 399, 410, 414, 427

9. 4,379,085, Apr. 5, 1983, Heat stabilization of plasma proteins; Craigenne A. Williams, et al., 530/381, 363, 380, 384, 393, 830

10. 4,296,134, Oct. 20, 1981, Liquid egg blend; Wayne A. Boldt, 426/250, 614

11. 4,272,523, Jun. 9, 1981, Fractionating citrate-stabilized plasma;

[illegible], et al., [illegible]

12. 4,092,438, May 30, 1978, Non-dairy coffee whitener containing acetate salt; George F. Tonner, 426/601, 613, 656, 658

13. 4,038,140, Jul. 26, 1977, Process for binding biologically active proteins; Dieter Jaworek, et al., 435/178, 180; 525/54.1, 54.31; 527/201, 202, 203, 313

14. 3,663,235, May 16, 1972, PROCESS OF PREPARING MARGARINE CONTAINING DIACYGLYCEROPHATIDE; Hans-Udo Menz, et al., 426/604; 252/309, 312, 356; 260/403 [IMAGE AVAILABLE]

=> d 2 kwic

US PAT NO: 4,806,524 L3: 2 of 14

SUMMARY:

BSUM(11)

Proteins used as erythropoietin stabilizers include bovine serum albumin and gelatin; sugars include monosaccharides such as xylose, mannose, glucose and fructose, disaccharides such as lactose,. . . and lysine; inorganic salts include potassium chloride, calcium chloride, sodium phosphate, potassium phosphate and sodium hydrogencarbonate; organic salts include sodium citrate , potassium citrate and sodium acetate; and sulfur-containing reducing agents include glutathione, thioctic acid, sodium thioglycolate, thioglycerol, .alpha.-monothioglycerol and sodium thiosulfate.

SUMMARY:

BSUM(17)

(1) . . . also indicated in the table. Each of the mixtures was distributed among 10 vials in amounts of 0.5 ml and freeze - dried . The 10 vials were divided into two groups, each consisting of 5 vials. The freeze - dried mixtures of one group were immediately dissolved in an aqueous solution containing 0.1% bovine serum albumin, 0.15M NaCl and 0.01M. . . The percentage of residual activity was determined, with the value for the first group (dissolved in aqueous solution immediately after freeze - drying) being taken as 100. The results are shown in the following table in the column of "Percentage of residual activity-- Freeze - dried ". Each of the figures in the column was a mean of five measurements. The data in the table show the. . .

DETDESC:

DETD(5)

An aqueous solution having the above composition was aseptically prepared, distributed among vials and freeze - dried , followed by the hermetic sealing of the vials.

DETDESC:

DETD(7)

A freeze - dried erythropoietin preparation was formulated as in Example 1 except that 100 parts by weight of gelatin was replaced by an. . .

DETDESC:

DETD(9)

A freeze - dried erythropoietin preparation was formulated as in Example 1 except that 100 parts by weight of gelatin was replaced by 500. . .

DETDESC:

DETD(16)

An aqueous solution having the above composition was aseptically prepared, distributed among vials and freeze - dried , followed by the hermetic sealing of the vials.

DETDESC:

DETD(18)

A freeze - dried erythropoietin preparation was formulated as in Example 4 except that the glycine and mannitol were replaced by 200 parts by. . .

DETDESC:

DETD(25)

An aqueous solution having the above composition was aseptically prepared, distributed among vials and freeze - dried , followed by the hermetic sealing of the vials.

DETDESC:

DETD(27)

A freeze - dried erythropoietin preparation was formulated as in Example 6 except that the glutathione and glucose were replaced by 10 parts by. . .

DETDESC:

DETD(41)

A . . . was dissolved in purified water to make a total of 10.sup.5 parts by weight, and the resulting aqueous solution was freeze - dried . The freeze - dried product was charged into capsules specified in the Japanese Pharmacopoeia, which were covered with an enteric coating agent by a. . .

=> d 3 kwic

US PAT NO: 4,803,073 L3: 3 of 14

SUMMARY:

BSUM(5)

There have already been several proposals that, to avoid these difficulties, plasma proteins be stabilized against the action of heat in aqueous solution by various additives such as amino acids, saccharides, sugar alcohols, Ca ions, potassium or ammonium citrate or salts of carboxylic acids and hydroxy carboxylic acids (compare, inter alia, U.S. Pat. Nos. 4,297,344, 4,440,679, 4,327,086 and 4,446,134,. . .

SUMMARY:

BSUM(7)

Processes . . . No. 4,490,361 is not entirely satisfactory since it is still necessary to accept considerable losses of activity. Thus, after a lyophilized AHF preparation has been heated in acetone, hexane or perfluorotripropylamine for ten hours, at a temperature in the region of. . .

SUMMARY:

BSUM(20)

The . . . fibrinogen, the proteins of the prothrombin complex, such as factors II, VII, IX and X, protein C, protein S, immunoglobulins, freeze - dried fresh plasma and the like. The preparation of these plasma proteins and the plasma protein fractions is known and has. . .

SUMMARY:

BSUM(21)

The . . . protein fractions are used for the pasteurization process according to the invention in dried form, as obtained, for example, by lyophilization , spray-drying or other non-damaging drying methods from the aqueous solutions of the plasma proteins which result from the fractionation. The. . .

DETDESC:

DETD(3)

1 g samples of freeze - dried preparation were taken from three production batches of factor VIII produced by known methods and one batch of freeze - dried fresh plasma (AHP), and each was mixed with 10 g of a commercially available dried sunflower oil at 60.degree. C.. . .

DETDESC:

DETD(19)

5 g of lyophilized fresh plasma (AHP) were pasteurized in 5 portions, as in example 1, with anhydrous corn oil at 60.degree. C. One. . .

DETDESC:

DETD(26)

2 g samples of three new batches of freeze - dried factor VIII preparations were pasteurized in 1 g portions as in example 1 using hardened vegetable fat at 60.degree. C.. . .

DETDESC:

DETD(29)

1 g samples of factor VIII powder from three freeze - dried factor VIII batches and freeze - dried fresh plasma (AHP) were pasteurized with dried lard as in example 1. The factor VIII values after the pasteurization were. . .

DETDESC:

DETD(32)

2 g of factor VIII or freeze - dried fresh plasma (AHP) were mixed in 1 g portions with 25 g portions of dried lard at 60.degree. C. 0.5. .

DETDESC:

DETD(38)

25 g portions of dried lard and 180 mg of CaCl2.2H.sub.2 O were added to 2 g of factor VIII or freeze - dried fresh plasma in 1 g portions at 60.degree. C., and the mixtures were pasteurized at 60.degree. C. for 21.5 hours.

DETDESC:

DETD(45)

1 g of lyophilized factor IX/PPSB-powder was mixed with 10 g corn oil. (The oil had been dried with anhydrous CaCl.sub.2 powder at 60.degree.. . .

DETDESC:

DETD(58)

Corn oil was dried as described in example 9. 1 g of lyophilized intramuscularly (i.m.) injectable gammaglobulin powder was suspended in 10 g dried corn oil. The suspension was pasteurized at 60.degree. C.. .
.

=> d 9 kwic

US PAT NO: 4,379,085 L3: 9 of 14

ABSTRACT:
A method for the heat stabilization of a plasma protein such as C1-INA or Factor IX comprising heating the protein in an aqueous medium in the presence of potassium or ammonium citrate in an amount of from in excess of 2.0 M to saturation of the medium. The method is particularly applicable to the stabilization of plasma proteins against thermal denaturation during pasteurization.

SUMMARY:

BSUM(7)

The invention encompasses a method for the heat stabilization of a plasma protein comprising heating the protein in the presence of potassium citrate or ammonium citrate . In particular, the invention includes a method for the pasteurization of a Factor IX or C1-INA plasma concentrate in the presence of ammonium or potassium citrate . The invention further includes a method for the preparation of a pasteurized C1-INA or Factor IX concentrate from plasma or. . . according to known protein separation techniques and heating the resultant partially purified fraction in the presence of potassium or ammonium citrate under conventional time and temperature pasteurizing conditions.

DETDESC:

DETD(2)

According to the invention, plasma proteins are stabilized against thermal denaturation by the presence of potassium or ammonium citrate in concentrations of from in excess of 2.0 M to saturation, preferably from about 2.5 M to saturation. Typically, a high molar citrate solution and/or citrate powder is added to an aqueous protein suspension in amounts sufficient to provide a citrate

preferably adjusted to about neutral with citric acid. Alternatively, a saturated or supersaturated solution of the citrate, is adjusted to a pH of about neutral with citric acid, and the protein sample added to the citrate to give the desired citrate concentration.

DETDESC:

DETD(6)

In . . . which case the saturation concentrations will be higher. For clinical use, the pasteurized C1-INA concentrate is then desalted, filtered and lyophilized according to known methods. Pasteurized Factor IX plasma concentrate is prepared by comparable purification techniques and pasteurization in the presence. . .

DETDESC:

DETD(9)

The . . . for small batches. The resultant concentrate is then pasteurized according to the process of the invention and desalted, filtered, and lyophilized to provide a C1-INA concentrate final product of intermediate purity, typically 60% to 150% purification over plasma at a yield. . .

DETDESC:

DETD(13)

After . . . concentrated to 0.02 plasma volume, and equilibrated with CS buffer by ultrafiltration. The product was then sterile filtered, dispensed and lyophilized to give an intermediate purity C1-INA product concentrate. Recovery of C1-INA was 29.4% of the C1-INA present in the starting. . .

DETDESC:

DETD(15)

Cryosupernatant . . . buffer, pH 6.8 (200 ml/l starting plasma). The CM eluate was then concentrated, equilibrated in CS, sterile filtered, filled, and lyophilized to give a product C1-INA concentrate of intermediate purity.

DETDESC:

DETD(17)

The . . . starting plasma). NaCl was added to isotonicity to the OH-Apatite unadsorbed fraction, and the isotonic product sterile filtered, filled and lyophilized to give a product C1-INA concentrate of high purity.

DETDESC:

DETD(19)

Alternatively, . . . is equilibrated and chromatographed according to Example 3, with addition of NaCl to isotonicity followed by sterile filtering, filling and lyophilization to give a high purity C1-INA product concentrate.

DETDESC:

DETD(24)

The . . . 200 ml with the PBS buffer, dispensed in 20 ml fills in 50 ml vials, frozen in liquid nitrogen, and lyophilized . The lyophilization cycle was 5 days and 16 hours. The product temperature during the prinary (sublimation) phase was maintained at -35.degree. C.,. . .

DETDESC:

DETD(27)

. . .

18.4 22.37

88.7

89.5

89.0

1.20 1.11

Assigned Value

*Control Sample

.sup.+ Lyophilized Sample from Example 1

CLAIMS:

CLMS(1)

What is claimed is:

1. A method for the heat stabilization of a plasma protein comprising heating the protein in an aqueous medium in the presence of ammonium or potassium citrate in an amount in excess of 2.0 M to saturation of the aqueous medium.

=> d 12 1-38

1. 4,938,856, Jul. 3, 1990, Process for mild heat treatment of a flowable fluid; Stratos E. Hatzidimitriu, 204/182.3, 131, 182.6; 426/239 [IMAGE AVAILABLE]

2. 4,917,685, Apr. 17, 1990, Delivery device for the administration of stabilized growth promoting hormones; Ravi Viswanathan, et al., 604/891.1; 530/399

3. 4,909,941, Mar. 20, 1990, High performance liquid chromatography mobile phase; Dick J. Poll, et al., 210/635, 542, 656; 530/305, 371, 399, 417 [IMAGE AVAILABLE]

4. 4,898,826, Feb. 6, 1990, Method to solubilize tissue plasminogen activator; Stephen A. Duffy, et al., 435/226; 424/94.64; 435/212, 219

5. 4,885,183, Dec. 5, 1989, Method for controlling melting properties of process cheese; John J. Strandholm, et al., 426/582, 583 [IMAGE AVAILABLE]

6. 4,880,751, Nov. 14, 1989, Immunoglobulin adsorption; William D. Georghegan, 436/518; 435/7.1; 436/512, 519, 525, 527, 529, 530, 531, 823; 530/388

7. 4,831,033, May 16, 1989, Use of amodiaquin in treatment of nervous system degeneration; Eugene Roberts, 514/255, 373

8. 4,816,568, Mar. 28, 1989, Stabilization of growth hormones; Edwin J. Hamilton, Jr., et al., 530/399; 514/970; 530/362, 363, 397

9. 4,806,537, Feb. 21, 1989, Use of amodiaquin and related compounds in treatment of nervous system degeneration; Eugene Roberts, 514/253

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s gonadotropin
L1          398 GONADOTROPIN#

=> s l1 and stabili?
        274440 STABI?
L2          356 L1 AND STABILI?

=> s l2 and (freeze dried or freeze drying or lyophilized or lyophilization)
         21742 FREEZE
        192525 DRIED
          5991 FREEZE DRIED
                 (FREEZE(W)DRIED)
         21742 FREEZE
        135912 DRYING
          4852 FREEZE DRYING
                 (FREEZE(W)DRYING)
          8260 LYOPHILIZED
          3504 LYOPHILIZATION
L3           175 L2 AND (FREEZE DRIED OR FREEZE DRYING OR LYOPHILIZED OR LYO
PHI
                 LIZATION)

=> s l3 and dicarboxylic acid#
         26395 DICARBOXYLIC
        279451 ACID#
         25161 DICARBOXYLIC ACID#
                 (DICARBOXYLIC(W)ACID#)
L4           10 L3 AND DICARBOXYLIC ACID#

=> d kwic

US PAT NO:      4,966,888 [IMAGE AVAILABLE]                L4: 1 of 10

SUMMARY:

BSUM(4)

 In . . . (active immunization), to a hormone critical to the
establishment and/or maintenance of pregnancy. The production and effects
of human chorionic  gonadotropin  (hCG) in pregnancy have singled out
hCG as a prime candidate for studies in immunological contraception. hCG
is not present. . .

DETDESC:

DETD(19)

 The . . . of protein components. Aliquots of 30-60 .mu.g of purified
fractions of the hLH-hCG receptor were solubilized in 0.5% Triton X-100,
 lyophilized  and dissolved in 100 .mu.l of water. Samples were then
dialyzed for 48 hours against 0.125 M Tris-HCl buffer (pH. . .

DETDESC:

DETD(26)

 From . . . ranges of about 34,000 to 38,000 and about 70,000 to
85,000. respectively, their specific binding capability for hCG and their
 stability  under the various conditions of treatment heretofore
described. In turn, these basic units appear to be linked through
covalent disulfide. . .

DETDESC:

DETD(48)

                 contained the reagent with hemagglutinin agglutinated
```

514/2,8,399

398 gonadotropin

which was concentrated by ultrafiltration through a PM-?? [illegible] and stored in a lyophilized state at 4.degree. C. until use.

DETDESC:

DETD(55)

Thus, . . . al. "Protein-Thiolation and Reversible Protein-Protein Conjugation", Biochem. J., 173:723 (1978), and Rebois et al, "Covalent Cross Linking of Human Chorionic Gonadotropin to Its Receptor in Rat Testes", Proc. Nat. Acad. Sci. U.S.A., Volume 78, No. 4, p. 2086 (Apr. 1981). Other. . . 2,4-diisocyanate. toluene 2,6-diisocyanate, 4.4.sup.1 -diisocyanatodiphenylmethane. hexane 1.6-disocyanate and the like. and bifunctional acylating agents such as di-acid halide, carboxylic dianhydrides, dicarboxylic acids, and esters and diamides, and imiidoesters, etc. may also be used.

DETDESC:

DETD(70)

It . . . employ silastic implants containing the receptor unit or receptor of the present invention. These implants can be used subdermally with lyophilized powder of the receptor unit or receptor. Body fluid such as plasma can pass through the silastic implant and pick. . .

DETDESC:

DETD(72)

The . . . to allow the silastic tubing to be completely filled with the receptor solution. The solution can then be frozen and lyophilized under sterile conditions. The resulting silastic implant will contain about 2.5 mg of the lyophilized receptor. The implants can be stored individually in free load trocars for implantation at 4.degree. C. in a dessicator under. . . of the present invention can last from 6-12 months in a human or animal and can be replenished with fresh lyophilized powder of the receptor unit or receptor if necessary.

DETDESC:

DETD(79)

The . . . of pH 8.5. The column was eluted with the same buffer. The gamma-globulin eluted in the unretarded protein fraction was lyophilized and stored at 4.degree. C. The protein concentration in the gamma-globulin fraction was determined by the method of Lowry, C.. . .

DETDESC:

DETD(82)

Highly . . . aliquot of 0.5 ml of 0.1M sodium phosphate buffer (pH 7.4. containing 0.1% Triton X-100) was added and mixed to stabilize the reaction mixture. The mixture was filtered through a 1.times.30 cm column of Ultrogel AcA-34 equilibrated with 0.1M sodium phosphate. . .

DETDESC:

DETD(84)

Inhibition . . . I-hCG to the plasma membrane receptor prepared from bovine Corpora lutea and rat Leydig cells. More specifically, approximately 125 ?g of lyophilized protein aliquots of the plasma

membranes were suspended in 100 .mu.l of distilled water and incubated at 4.degree. C. with. . .

CLAIMS:

CLMS(1)

We . . .

animal to selectively induce an antibody response comprising:
(A) a first unit selected from the group consisting of
(i) human chorionic gonadotropin . and
(ii) a .beta.-subunit of human chorionic gonadotropin . and
(B) a second unit comprising a purified receptor for human chorionic gonadotropin conjugated with said first unit, said antigen being capable of selectively inducing an antibody response to each of said first. . .

CLAIMS:

CLMS(2)

2. The antigen of claim 1 wherein the antigen comprises the .beta.-subunit of human chorionic gonadotropin .

CLAIMS:

CLMS(3)

3. . . . the second unit of the antigen comprises a purified fraction of an extract containing the naturally-occurring receptor for human chorionic gonadotropin .

CLAIMS:

CLMS(4)

4. . . . the extract is of a plasma membrane of a corpus luteum of a species containing the receptor for human chorionic gonadotropin .

CLAIMS:

CLMS(20)

20. A vaccine for preventing pregnancy comprising in combination in an amount sufficient for preventing pregnancy (1) human chorionic gonadotropin or the .beta.-subunit of human chorionic gonadotropin as an antigen capable of selectively generating antibodies comprising determinants for human chorionic gonadotropin , and (2) a purified receptor for human chorionic gonadotropin as an antigen capable of selectively generating antibodies comprising determinants for the naturally-occurring receptor for human chorionic gonadotropin , and a pharmaceutically acceptable carrier.

CLAIMS:

CLMS(22)

22. A vaccine for preventing pregnancy comprising in an amount effective for preventing pregnancy a purified naturally-occurring receptor for human chorionic gonadotropin as an antinen capable of selectively generating antibodies comprising determinants for the naturally-occurring receptor for human chorionic gonadotropin and a pharmaceutically acceptable carrier.

=> d 1-10

1. 4,966,888, Oct. 30, 1990, hCG-hLH receptor and hCG-hLH receptor-hCG complex as antigens, antibodies thereto and contraceptive vaccine; Brij B. Saxena, et al., 514/2; 424/88; 435/70.1, 70.3; 514/8, 12; 530/350, 398, 399 [IMAGE AVAILABLE]

2. 4,906,749, Mar. 6, 1990, Cyclic anhydride derivatives of chromophors; Spyros Theodoropulos, 424/1.1, 9; 435/4, 5, 968; 436/500, 532; 526/204; 530/363, 391, 405, 409; 544/99, 103, 229, 237 [IMAGE AVAILABLE]

3. 4,889,861, Dec. 26, 1989, Substituted imidazo[1,5-a]pyridine derivatives and other substituted bicyclic derivatives and their use as aromatase inhibitors; Leslie J. Browne, 514/300, 228.2, 233.2, 252; 544/61, 127, 362; 546/121

4. 4,822,878, Apr. 18, 1989, Cyclic anhydride derivatives of chromophors; Spyros Theodoropulos, 544/99, 31, 37, 103, 227, 237; 546/107; 549/225, 232, 234, 237, 240, 244

5. 4,792,521, Dec. 20, 1988, Non-enzymatic immunohistochemical staining system and reagents; Dan Shochat, 435/7.23; 424/3, 5, 7.1; 435/5, 7.21, 7.22, 7.32, 7.4, 810, 960; 436/501, 512, 519

6. 4,728,645, Mar. 1, 1988, Substituted imidazo[1,5-A]pyridine derivatives and other substituted bicyclic derivatives, useful as aromatase inhibitors; Leslie J. Browne, 514/214, 210, 228.2, 233.2, 253, 393; 540/303, 476, 579; 544/51, 139, 199, 370; 548/324

7. 4,687,732, Aug. 18, 1987, Visualization polymers and their application to diagnostic medicine; David C. Ward, et al., 435/6, 7.4, 7.5, 7.72, 7.9, 14, 21, 25, 28, 188, 810, 968, 975; 436/501, 504, 537, 545, 546, 800, 801, 804, 808, 827

8. 4,617,307, Oct. 14, 1986, Substituted imidazo[1,5-A]pyridine derivatives as aromatase inhibitors; Leslie J. Browne, 514/300; 546/121

9. 4,483,921, Nov. 20, 1984, Immunoassay with antigen or antibody labeled liposomes sequestering enzyme; Francis X. Cole, 435/7.9, 177, 182, 188, 810, 966, 975; 436/536, 537, 829 [IMAGE AVAILABLE]

10. 4,342,826, Aug. 3, 1982, Immunoassay products and methods; Francis X. Cole, 435/7.9, 177, 182, 188, 810, 966, 975; 436/829 [IMAGE AVAILABLE]

=>
=> s l2 and (citric or citrate or tartaric or tartarate or tartrate or aspartic or aspartate)
28589 CITRIC
18704 CITRATE
17067 TARTARIC
802 TARTARATE
8496 TARTRATE
4581 ASPARTIC
1002 ASPARTATE
L5 158 L2 AND (CITRIC OR CITRATE OR TARTARIC OR TARTARATE OR TARTRATE OR ASPARTIC OR ASPARTATE)

=> d kwic

US PAT NO: 5,024,998 L5: 1 of 158

SUMMARY:

BSUM(7)

two points in space in accordance with selectively variable override values, each override value corresponding to a ratio, expressed as a percentage, of the desired velocity of movement of the machine element to a . . . velocity, wherein the improvement comprises: . . .predetermining for each axis a distance-time curve at the normal operating velocity, corresponding to an override value of 100%, between the points in space, and determining an instantaneous distance-time curve for moving the machine part so as to. . . . override values for each axis, a time expansion of the predetermined distance-time curve that is inversely proportional to the respective override value .ride values for each axis, a time expansion of the predetermined distance-time curve that is inversely proportional to the respective override value .pping point as the velocity profile for 100% override. protect. . . e sign 1 for several years, it is preferable to provide an abrasion resistant elastic covering sheet or coating 3 to protect. . . vision, wherein said marking device is mounted on one of said ocular supports and comprises a mounting member adapted for detachable mounting on said ocular support and an upper member for supporting said light-emitting surface, said upper member being pivotably attached. . . not be converted to a silicide. It is then possible to chemically remove the metal but not the silicide by etching in an environment where the metal but not the silicide is etched . In an example where the metal is platinum, the etch can be accomplished by exposing the surface to an acid such as aqua regia which removes the metal but does not etch the oxide or the silicide. As illustrated, no silicide forms on the gate spacer 451' but, due to silicide formation. . . yarn has an elongation between 45% and 150%.

According to further aspects of the invention, the preferred polyamide is nylon 66 . Preferably the branching agent constitutes between 0.01 and 1 mol percent of the polymer, and it is especially preferred that. . . 1.75. If the polymer is to be melted on a conventional grid prior to the step of extruding, the polymer RV is advantageously less than 60 (preferably between 40 and 55). while if an extruder is used to melt the polymer, the polymer RV is preferably between 50 and 80.

	0.25	0.60	0.40	0.30	0.25	0.30
sheet (mm)						
Method of roughening						
	polishing with					
		Scotch shot blast-				
			polish-			
				Scotch Scotch		
the surface of metal						
	sand paper					
		brighten-				
		ing	ing with			
				brighten-		
					brightening	
sheet		ing		sand paper		
				ing		
Chemical conversion						
	phosphating					
		phosphating				
			phosphating			
				untreated		
				phosphating		
					phosphating	
process						
Type of. . .	5	6	--			
nate added (phr)						
Type of flaky filler						
	none	sericite				
		chlorite				
			talc	none	--	

surface

graphite base

graphite

none none graphite

graphite

layer base base base

Cure conditions

200.degree. C.. . .

SUMMARY:

BSUM(8)

Matsuyama . . . Koho JP No. 59/104556 (84/104556), published June 16, 1984, cyclized oligosaccharides such as .beta.-cyclodextrin have been recently used in protein stabilizers which prevent denaturation of proteins and enzymes in blood. Human blood mixed with octylphenoxypoly(ethoxyethanol) and .beta.-cyclodextrin was maintained for 24. . .

SUMMARY:

BSUM(11)

Hydroxypropyl-.beta.-cyclodextrin . . . 987-990, concerning the same and related studies. Pitha et al also describe in the J. Pharm. Sci. article the storage stability of tablets containing a testosteronehydroxypropyl-.beta.-cyclodextrin complex and the lack of toxicity of the cyclodextrin itself. as well as the importance. . .

SUMMARY:

BSUM(12)

The . . . That patent claims a composition containing an amorphous complex of cyclodextrin and a drug, and a method of producing a stabilizing amorphous complex of a drug and a mixture of cyclodextrins comprising (1) dissolving an intrinsically amorphous mixture of cyclodextrin derivatives. . .

SUMMARY:

BSUM(20)

The . . . and other hydrophilic cyclodextrin derivatives, including enhanced drug absorption. The mechanism of enhancing drug absorption is described and the apparent stability constants for inclusion complexes of various drugs with .beta.-cyclodextrin, dimethyl-.beta.-cyclodextrin, hydroxypropyl-.beta.-cyclodextrin and maltosyl-.beta.-cyclodextrin are given. Drugs studied with these cyclodextrins. . .

SUMMARY:

BSUM(34)

Japanese . . . 1987, describes production of glucose and maltooligosaccharide (2-4 glucose units) derivatives of .alpha.-, .beta.- and .gamma.-cyclodextrin and their use as stabilizers for pharmaceuticals.

SUMMARY:

BSUM(41)

The . . . appropriate high levels, the initial lung to brain levels are high as well. Still further, the dihydropyridine-containing

derivatives suffer from stability problems, since even in the dry state they are very sensitive to oxidation as well as to water addition. These. . .

SUMMARY:

BSUM(42)

Applicant's parent U.S. Pat. application Ser. No. 07/139,755, filed Dec. 30, 1987, incorporated by reference herein, relates to a method for stabilizing the reduced, dihydropyridine forms of dihydropyridine.revreaction.pyridinium salt redox systems for brain-targeted drug delivery by forming inclusion complexes of the dihydropyridine. . .

SUMMARY:

BSUM(44)

Applicant's parent U.S. patent application Ser. No. 07/431,222, filed Nov. 3, 1989, incorporated by reference herein, relates to a method for stabilizing the reduced, dihydropyridine forms of dihydropyridine.revreaction.pyridinium salt redox systems for brain-targeted drug delivery by forming inclusion complexes of the dihydropyridine. . .

DETDESC:

DETD(4)

Numerous drugs suffer from problems associated with their lack of water solubility and/or lack of stability in water. These lipophilic and/or water-labile drugs cannot be practically formulated as aqueous parenteral solutions. Consequently, the drugs are either. . .

DETDESC:

DETD(28)

Other . . . cancer treatment; vincristine and vinblastine, anticancer alkaloids; hydroxyurea and DON, anticancer urea derivatives; FSH, HCG and HCS, pituitary and nonpituitary nonadotropins, used, for example, in certain reproductive disorders; N,N'-bis(dichloracetyl)-1,8-octamethylenediamine (fertilysin), an agent for male fertility inhibition; levorphanol, a narcotic analgesic; benzestrol. . .

DETDESC:

DETD(29)

Preferred . . . be mentioned amino acids, such as GABA, GABA derivatives and other omega-amino acids, as well as glycine, glutamic acid, tyrosine, aspartic acid and other natural amino acids; catecholamines, such as dopamine, norepinephrine and epinephrine; serotonin, histamine and tryptamine; and peptides such. . .

DETDESC:

DETD(34)

The . . . nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, fumaric, methanesulfonic, toluenesulfonic and the like. The expression "anion of

4. . .

DETDESC:

DETD(78)

As . . . units (.alpha.=six, .beta.=seven, .gamma.=eight) determine the size of a cone-like cavity which is amenable to inclusion by many drugs. The _stability_ of the complex formed depends on the fit of the drug into the cyclodextrin and the cyclodextrin concentration. Unfortunately, the. . .

DETDESC:

DETD(82)

In . . . molecular weight of the mixture) gave a line with a slope of 0.2. This is an estimation of the bulk _stability_ of the cyclodextrin complex and compares reasonably with other systems.

DETDESC:

DETD(120)

Standard solutions and _stability_

DETDESC:

DETD(122)

Dihydropyridine derivatives like E.sub.2 -CDS are known to be easily oxidized and very labile in acidic solutions. The _stability_ of E.sub.2 -CDS was investigated under different conditions at room temperature. These studies were performed by diluting the E.sub.2 -CDS. . .

DETDESC:

DETD(134)

Complexation . . . 2-hydroxypropyl-.beta.-cyclodextrin (HPCD) or other selected cyclodextrin derivative as defined herein has been found to be particularly advantageous in that it _stabilizes_ the dihydropyridine redox systems. A direct comparison of _stabilities_ in aqueous solution is, of course, not possible because of the low solubility of the dihydropyridine redox system drugs in. . .

=> o

=> s l5 and sugar#
35602 SUGAR#
L6 66 L5 AND SUGAR#

=> s l6 and (surfactant# or detergent#)
41141 SURFACTANT#
25079 DETERGENT#
L7 13 L6 AND (SURFACTANT# OR DETERGENT#)

=> d 1-13

1. 4,997,772, Mar. 5, 1991, Water-insoluble particle and immunoreactive reagent, analytical elements and methods of use; Richard C. Sutton, et al., 436/533; 422/56; 435/5, 7.34, 36; 436/534; 523/201; 525/902 [IMAGE AVAILABLE]

2. 4,976,644, Dec. 18, 1990, Method of detecting a substance using

enzymatically-induced decomposition of dioxetanes; Irena Y. Gronstein 435/21, 5, 26, 29, 120, 810; 536/27 [IMAGE AVAILABLE]

3. 4,966,855, Oct. 30, 1990, hCG-hLH receptor and hCG-hLH receptor-hCG complex as antigens, antibodies thereto and contraceptive vaccines; Brij B. Saxena, et al., 514/2; 424/88; 435/70.1, 70.3; 514/8, 12; 530/350, 398, 399 [IMAGE AVAILABLE]

4. 4,966,856, Oct. 30, 1990, Analytical element and the analytical method using the element; Tsukasa Ito, et al., 436/170; 422/56, 57, 58; 435/4, 7.8, 7.93, 28, 805, 970; 436/172, 804, 805 [IMAGE AVAILABLE]

5. 4,957,494, Sep. 18, 1990, Multi-layer delivery system; Patrick S. L. Wong, et al., 604/892.1, 121, 891.1 [IMAGE AVAILABLE]

6. 4,931,385, Jun. 5, 1990, Enzyme immunoassays and immunoloric reagents; Elliott Block, et al., 435/7.94, 28, 188, 805, 810, 975; 436/518, 808, 810, 814, 818, 826 [IMAGE AVAILABLE]

7. 4,880,914, Nov. 14, 1989, Assay for qualitatively and/or quantitatively measuring hLH or hCG in body fluids and reagents therefor; Brij B. Saxena, et al., 530/395; 424/88; 514/8; 530/397, 398, 412, 413 [IMAGE AVAILABLE]

8. 4,868,106, Sep. 19, 1989, Analytical element and method for determining a component in a test sample; Tsukasa Ito, et al., 435/7.7; 422/56, 57; 435/7.5, 7.71, 7.72, 7.8, 7.92, 7.94, 805, 968; 436/501, 518, 524, 527, 528, 529, 530, 531, 800, 810, 827, 828

9. 4,801,577, Jan. 31, 1989, Nonapeptide and decapeptide analogs of LHRH useful as LHRH antagonists; John J. Nestor, Jr., et al., 514/15, 800; 530/313, 328; 930/20, 21, 23, 130, DIG.803

10. 4,560,649, Dec. 24, 1985, Assaying for hLH or hCG with immobilized hormone receptors; Brij B. Saxena, et al., 435/7.21, 7.8, 7.92, 181, 188, 810, 961, 963, 964, 975; 436/501, 527, 805, 810, 817, 818; 530/313, 397, 398, 399, 812

11. 4,501,692, Feb. 26, 1985, Charge effects in enzyme immunoassays; Ian Gibbons, et al., 530/389; 424/530; 436/547; 530/390

12. 4,287,300, Sep. 1, 1981, Charge effects in enzyme immunoassays; Ian Gibbons, et al., 435/5, 7.32, 7.9, 188, 810; 436/527, 529, 531, 546, 547, 800, 805, 806, 811, 815, 820

13. 4,208,479, Jun. 17, 1980, Label modified immunoassays; Robert F. Zuk, et al., 435/7.9, 7.72, 7.8; 436/512, 537, 808, 825

s l3 and (aspartic or aspartate or citric or citrate or tartaric or tartrate or tartarate)

	4581	ASPARTIC
	1002	ASPARTATE
	28589	CITRIC
	1A704	CITRATE
	17087	TARTARIC
	8496	TARTRATE
	592	TARTARATE
L6	88	L3 AND (ASPARTIC OR ASPARTATE OR CITRIC OR CITRATE OR TARTARIC OR TARTRATE OR TARTARATE)

=> d 40 kwic

US PAT NO: 4,751,004 L8: 40 of 88

SUMMARY:

BSUM(8)

Moreover, . . . in general, that glycosylation can cause certain differences in the protein of which the following are of biological interest: antigenicity, stability, solubility and tertiary structure. The carbohydrate side-chains also can affect the protein's half-life and target it to receptors on the. . .

SUMMARY:

BSUM(14)

Another . . . which biological activity resides in the oligosaccharide moieties (i.e., particular structure at a specific site) is that of human chorionic gonadotropin (hCG). Thus, it is known that hCG without carbohydrate is a competitive inhibitor of native hCG; that oligosaccharides isolated from. . .

SUMMARY:

BSUM(27)

Determination . . . glycosylated t-PA from the protein backbone and any of these oligosaccharides. Modified t-PA glycoproteins can thus be prepared with varying stability, solubility, activity and other such properties. The serum half-life of the t-PA also can be extended by attaching certain terminal. . .

DETDESC:

DETD(29)

In . . . de Werf et al., Circulation 69(3), 605-613 (1984). An occlusive thrombus formed at the site of the coil. Presence and stability of the clot was confirmed by angiography. A 50 ml syringe pump was used to infuse t-PA solution via a. . .

DETDESC:

DETD(49)

The . . . were collected. The peak fractions (650 ml volume) were dialyzed against three 10 liter portions of 0.01% Tween 80 and lyophilized .

DETDESC:

DETD(51)

The lyophilized peak fractions from Con A-Sepharose chromatography were dissolved in a minimum volume of H.sub.2 O (21 ml final volume) and. . .

DETDESC:

DETD(55)

Since . . . 0.5 ml were collected and the peak fractions (1.5 ml) represented the final product. One ml of this solution was lyophilized directly in the glass tube used for hydrazinolysis and submitted for oligosaccharide analysis.

DETDESC:

DETD(197)

The . . . for sample A. Recovery was 1.3 mg of t-PA in 2.0 ml volume. One ml of the final preparation was lyophilized in a hydrazinolysis tube and used for oligosaccharide analysis.

DETDESC:

DETD(773)

Radioactive . . . exoglycosidase will hydrolyse 1 mole of the synthetic substrate per minute). (i) jack bean .beta.-galactosidase: 6 units ml.sup.-1 in 0.1M citrate /phosphate buffer, pH 4.0; (ii) jack bean .beta.-N-acetylhexosaminidase: 10 units ml.sup.-1 in 0.1M citrate buffer, pH 5.0; (iii) Streptococcus pneumoniae .beta.-N-acetylhexosaminidase: 0.2 units ml.sup.-1 in 0.1M citrate phosphate buffer, pH 6.0; (iv) jack bean .alpha.-mannosidase: 10 units ml.sup.-1 in 0.1M acetate buffer, pH 5.0; (v) Aspergillus phoenicis. . . .alpha.1.fwdarw.2 mannosidase: 5 .mu.g ml.sup.-1 in 0.1M acetate buffer, pH 5.0; (vi) bovine epidydimal .alpha.-fucosidase: 2 units ml.sup.-1 in 0.2M citrate /phosphate buffer, pH 6.0; (vii) snail .beta.-mannosidase: 0.5 units ml.sup.-1 in 0.5M citrate buffer, pH 4.5; (viii) Arthrobacter ureafaciens neuraminidase: 10 units ml.sup.-1 in 0.1M acetate buffer, pH 5.0. All digestions were performed. . .

DETDESC:

DETD(190)

Preparation of tryptic peptides. A portion of the above preparation of colon-t-PA (C-tPA) (4.5 ml volume, about 0.64 mg protein) was lyophilized . A similar amount of Bowes melanoma t-PA (B-tPA) (0.645 ml of a 0.93 mg/ml solution in 1M NH.sub.4 HCO.sub.3, purchased from American Diagnostica, Inc., product number 110, lot 16-01), was diluted to 4.0 ml with 1M NH.sub.4 HCO.sub.3 and lyophilized . The lyophilized C-tPA and B-tPA samples were then dissolved in 1 ml of 0.1M Tris-HCl, pH 8.15, 6M guanidine-HCl, 2 mM EDTA, . . . samples were then desalted by gel filtration over small columns of Sephadex G-25 equilibrated with 1M NH.sub.4 HCO.sub.3 and lyophilized .

DETDESC:

DETD(191)

The carboxymethylated, lyophilized samples were then each dissolved in 2 ml of 0.1M NH.sub.4 HCO.sub.3 and digested for 10 hr at room temperature. . . 17.8 .mu.g (C-tPA sample) or 15.7 .mu.g (B-tPA sample) of TPCK-treated trypsin (Sigma Chemical Co.). The trypsinized samples were then lyophilized . The lyophilized glycopeptides were dissolved in 1 ml of 0.1% trifluoroacetic acid (TFA) and subjected to reversed-phase HPLC. HPLC conditions were as. . .

DETDESC:

DETD(205)

Thermal Stability

DETDESC:

DETD(206)

The comparative stabilities of colon t-PA and melanoma t-PA were examined under a variety of temperature conditions and buffer compositions at about neutral. . . depending upon the conditions used. Since the main acid sequences of the two t-PA products are alike, the

differences in stability were deemed to be due to the carbohydrate structure. In another test run under selected assay conditions at a relatively. . .

DETDESC:

DETD(207)

In these stability tests the various temperature and buffer conditions used were: (1) 60.degree. C. for 10 hours in phosphate buffered saline containing. . .

DETDESC:

DETD(208)

The stability test results were obtained by several assay methods: amidolytic, parabolic and fibrin plate assays. In the amidolytic assay, hydrolysis of. . .

=) d acc 4751084

1. 4,751,084, Jun. 14, 1988, Tissue plasminogen activator from normal human colon cells: Joseph Feder, et al., 424/94.64, 94.63; 435/212, 219; 514/8, 54, 822; 530/395; 536/123

=) d 1-88

1. 5,024,998, Jun. 18, 1991, Pharmaceutical formulations for parenteral use: Nicholas S. Bodor, 514/58; 424/1.1, 85.8, 94.1; 514/777, 937; 536/103

2. 5,019,383, May 28, 1991, Fatty acid carriers for synthetic peptides; Thomas P. Hopp, 424/88; 530/345, 406 [IMAGE AVAILABLE]

3. 5,017,566, May 21, 1991, Redox systems for brain-targeted drug delivery: Nicholas S. Bodor, 514/58, 964, 965; 536/103 [IMAGE AVAILABLE]

4. 5,013,831, May 7, 1991, Detectable molecules, method of preparation and use: Jannis G. Stavrianopoulos, 536/27; 435/6; 536/28, 29 [IMAGE AVAILABLE]

5. 5,013,757, May 7, 1991, Physiologically active substance Tan-931, its derivatives, their production and use; Tsuneo Kanamaru, et al., 514/568; 544/3, 8, 174, 176, 391; 546/226; 548/127, 128, 214, 578; 560/56; 562/440, 441, 460; 564/167, 169 [IMAGE AVAILABLE]

6. 5,013,713, May 7, 1991, Prolonged release of biologically active somatotropin: James W. Mitchell, 514/2, 6, 12, 21; 530/399 [IMAGE AVAILABLE]

7. 5,002,935, Mar. 26, 1991, Improvements in redox systems for brain-targeted drug delivery; Nicholas S. Bodor, 514/58; 424/488; 514/778, 965; 536/103 [IMAGE AVAILABLE]

8. 5,002,885, Mar. 26, 1991, Detectable molecules, method preparation and use: Jannis G. Stavrianopoulos, 435/188, 6, 7.5, 7.9, 7.92; 435/548; 530/350, 387, 389, 390, 391, 402; 536/1.1, 27, 28, 29, 55.1, 56, 102 [IMAGE AVAILABLE]

9. 4,985,404, Jan. 15, 1991, Prolonged release of biologically active polypeptides: James W. Mitchell, 514/6, 2, 12, 21, 492, 494, 499, 501, 502, 503, 505; 530/399, 400 [IMAGE AVAILABLE]

10. 4,983,596, Jan. 8, 1991, Pharmaceutical formulations for parenteral use: Nicholas S. Bodor, 514/58, 777; 536/103 [IMAGE AVAILABLE]

11. 4,978,672, Dec. 18, 1990, Alpha-heterocycle substituted tolunitriles; Robert M. Bowman, et al., 514/383, 333, 340; 546/256, 276; 548/262.2 [IMAGE AVAILABLE]

12. 4,976,957, Dec. 11, 1990, Process for the production of recognins and their chemoreciprocals; Samuel Bogoch, 424/86, 85.8, 573; 436/530, 542, 547; 530/388, 814 [IMAGE AVAILABLE]

13. 4,966,888, Oct. 30, 1990, hCG-hLH receptor and hCG-hLH receptor-hCG complex as antigens, antibodies thereto and contraceptive vaccine; Brij B. Saxena, et al., 514/2; 424/88; 435/70.1, 70.3; 514/8, 12; 530/350, 39A, 399 [IMAGE AVAILABLE]

14. 4,962,091, Oct. 9, 1990, Controlled release of macromolecular polypeptides; Deborah A. Eppstein, et al., 514/2; 424/78, 85.1, 85.2, 85.4, 85.6, 85.8, 89, 92; 514/21, 964 [IMAGE AVAILABLE]

15. 4,954,298, Sep. 4, 1990, Method for producing microcapsule; Masaki Yamamoto, et al., 264/4.6, 4.1; 424/461, 462, 493, 497; 514/800, 885, 963; 604/891.1 [IMAGE AVAILABLE]

16. 4,952,685, Aug. 28, 1990, Detectable molecules, method of preparation and use; Jannis G. Stavrianopoulos, 536/27; 435/6; 534/551, 775; 536/28, 29 [IMAGE AVAILABLE]

17. 4,943,523, Jul. 24, 1990, Detectable molecules, method of preparation and use; Jannis G. Stavrianopoulos, 435/7.5; 436/537, 804; 530/390; 534/11, 12, 13, 14; 536/17.1 [IMAGE AVAILABLE]

18. 4,937,250, Jun. 26, 1990, Alpha-heterocycle substituted tolunitriles; Robert M. Bowman, et al., 514/341, 399; 546/278; 548/335 [IMAGE AVAILABLE]

19. 4,935,543, Jun. 19, 1990, Physiologically active substance tan-931, its derivatives, their production and use; Tsuneo Kanamaru, et al., 564/169; 544/3, 8, 174, 176, 391; 546/226; 548/127, 128, 214, 578; 560/56; 562/440, 441, 460; 564/167 [IMAGE AVAILABLE]

20. 4,931,385, Jun. 5, 1990, Enzyme immunoassays and immunologic reagents; Elliott Block, et al., 435/7.94, 28, 188, 805, 810, 975; 436/518, 808, 810, 814, 818, 826 [IMAGE AVAILABLE]

21. 4,917,893, Apr. 17, 1990, Prolonged release microcapsules; Hiroaki Okada, et al., 424/423, 433, 497, 499, 500; 428/402.2; 514/2, 800, 843, 963 [IMAGE AVAILABLE]

22. 4,914,189, Apr. 3, 1990, Synthetic GHRH analogs; Andrew V. Schally, et al., 530/324 [IMAGE AVAILABLE]

23. 4,912,034, Mar. 27, 1990, Immunoassay test device and method; Krishan L. Kalra, et al., 435/7.92; 422/56, 58, 61, 101; 435/4, 7.5, 805; 436/501, 518, 524, 528, 531, 548, 807, 808, 817, 824

24. 4,889,861, Dec. 26, 1989, Substituted imidazo[1,5-a]pyridine derivatives and other substituted bicyclic derivatives and their use as aromatase inhibitors; Leslie J. Browne, 514/300, 228.2, 233.2, 252; 544/61, 127, 362; 546/121

25. 4,880,914, Nov. 14, 1989, Assay for qualitatively and/or quantitatively measuring hLH or hCG in body fluids and reagents therefor; Brij B. Saxena, et al., 530/395; 424/88; 514/8; 530/397, 398, 412, 413 [IMAGE AVAILABLE]

26. 4,879,249, Nov. 7, 1989, Linker compounds, linker-compound-ligands and linker-ligand-reagents; Thomas P. Baldwin, et al., 436/543,

475/168; 436/544; 546/261; 548/475; 558/6, 15, 397, 437; 560/307; 562/512; 564/300; 568/22

27. 4,868,106, Sep. 19, 1989, Analytical element and method for determining a component in a test sample; Tsukasa Ito, et al., 435/7.7; 422/56, 57; 435/7.5, 7.71, 7.72, 7.8, 7.92, 7.94, 805, 968; 436/501, 518, 524, 527, 528, 529, 530, 531, 800, 810, 827, 828

28. 4,851,517, Jul. 25, 1989, Tissue plasminogen activator oligosaccharide from normal human colon cells; Joseph Feder, et al., 536/1.1, 53, 123

29. 4,849,505, Jul. 18, 1989, Detectable molecules, method of preparation and use; Jannis G. Stavrianopoulos, 530/300; 424/1.1; 435/5, 6, 7.21, 7.5, 180; 436/518, 531, 532; 530/350, 402, 405; 536/26, 27, 55.1 [IMAGE AVAILABLE]

30. 4,849,208, Jul. 18, 1989, Detectable molecules, method of preparation and use; Jannis G. Stavrianopoulos, 424/1.1; 128/654, 659; 424/9; 600/3 [IMAGE AVAILABLE]

31. 4,843,122, Jun. 27, 1989, Detectable molecules, method of preparation and use; Jannis G. Stavrianopoulos, 525/61, 331.3, 333.2, 376, 453; 530/300, 345, 350, 402, 405; 536/1.1, 26, 27, 55.1

32. 4,840,915, Jun. 20, 1989, Method for diagnosing malignant tumors; Samuel Bopoch, 436/530, 543, 805, 811, 813, 824

33. 4,824,784, Apr. 25, 1989, Chromogenic solution for immunoassay; Walter D. Cantarow, 435/7.94, 7.5, 28, 188, 810, 963; 436/66

34. 4,801,577, Jan. 31, 1989, Nonapeptide and decapeptide analogs of LHRH useful as LHRH antagonists; John J. Nestor, Jr., et al., 514/15, 800; 530/313, 328; 930/20, 21, 23, 130, DIG.803

35. 4,798,885, Jan. 17, 1989, Compositions of hormonally active human and porcine inhibin containing an .alpha. chain and 62 chain; Anthony J. Mason, et al., 530/350; 930/10, 260, DIG.530, DIG.821

36. 4,792,521, Dec. 20, 1988, Non-enzymatic immunohistochemical staining system and reagents; Dan Shochat, 435/7.23; 424/3, 5, 7.1; 435/5, 7.21, 7.22, 7.32, 7.4, 810, 960; 436/501, 512, 519

37. 4,785,080, Nov. 15, 1988, Labeled analytes; Peter R. Farina, et al., 530/402; 435/7.23, 7.4, 7.9, 188, 199, 207; 530/300, 307, 308, 313, 316, 323, 350, 388, 390, 399, 403, 404, 405, 406; 930/10, 240

38. 4,782,137, Nov. 1, 1988, Synthesis of protein with an identification peptide, and hybrid polypeptide incorporating same; Thomas P. Hopp, et al., 530/328; 435/69.3, 69.7; 530/330, 350; 930/10, 20

39. 4,774,192, Sep. 27, 1988, A dry reagent delivery system with membrane having porosity gradient; Louis Terminiello, et al., 436/530; 422/56; 435/11, 12, 14, 22, 25, 805, 810; 436/518, 531, 808, 810, 817, 901

40. 4,751,084, Jun. 14, 1988, Tissue plasminogen activator from normal human colon cells; Joseph Feder, et al., 424/94.64, 94.63; 435/212, 219; 514/8, 54, 822; 530/395; 536/123

41. 4,749,713, Jun. 7, 1988, Alpha-heterocycle substituted tolunitriles; Robert M. Bowman, et al., 514/341, 339, 396, 397, 399; 546/256, 273, 278; 548/335, 336

42. 4,737,456, Apr. 12, 1988, Reducing interference in ligand-receptor binding assays; Litai Weng, et al., 435/7.92, 4, 810, 962, 975; 436/500,

514, 537, 547, 548, 808, 817, 818, 819, 825; 935/108, 110

43. 4,726,645, Mar. 1, 1988, Substituted imidazo[1,5-A]pyridine derivatives and other substituted bicyclic derivatives, useful as aromatase inhibitors; Leslie J. Browne, 514/214, 210, 220.2, 233.2, 253, 393; 540/303, 476, 579; 544/61, 139, 199, 370; 548/324

44. 4,727,024, Feb. 23, 1988, Binding assays involving formation and detection of light scattering crystals; Martin Koocher, et al., 435/7.4, 7.8, 810; 436/36, 501, 518, 525, 536, 805, 808, 809

45. 4,722,889, Feb. 2, 1988, Immunoassays using multiple monoclonal antibodies and scavenger antibodies; Jin P. Lee, et al., 435/7.94, 28, 188, 810, 962, 971, 975; 436/518, 531, 532, 533, 534, 539, 540, 548; 935/110 [IMAGE AVAILABLE]

46. 4,711,782, Dec. 8, 1987, Prolonged release microcapsules and their production; Hiroaki Okada, et al., 424/455; 264/4.6; 424/457, 497; 428/402.2; 514/963 [IMAGE AVAILABLE]

47. 4,707,440, Nov. 17, 1987, Nucleic acid hybridization assay and detectable molecules useful in such assay; Jannis G. Stavrianopoulos, 435/6; 536/26, 27; 935/78 [IMAGE AVAILABLE]

48. 4,705,778, Nov. 10, 1987, Orally active LHRH analogs; Ronald G. Almquist, et al., 514/15, A00; 530/313; 930/20, 21, 130, DIG.692, DIG.693, DIG.696, DIG.697

49. 4,703,004, Oct. 27, 1987, Synthesis of protein with an identification peptide; Thomas P. Hopp, et al., 435/69.7, 172.3, 320.1; 536/27; 930/10, 20, 280

50. 4,692,452, Sep. 8, 1987, Method for treatment of endometritis in mammalian females; Antonin Cerny, et al., 514/288

51. 4,687,732, Aug. 18, 1987, Visualization polymers and their application to diagnostic medicine; David C. Ward, et al., 435/6, 7.4, 7.5, 7.72, 7.9, 14, 21, 25, 28, 188, 810, 968, 975; 436/501, 504, 537, 545, 546, 800, 801, 804, 808, 827

52. 4,670,419, Jun. 2, 1987, Pharmaceutical composition and its rectal use; Yoshiaki Uda, et al., 514/16, 17, 18, 19, 800, 806, 807, 809; 930/20, 21, 130

53. 4,668,619, May 26, 1987, Multilayer homogeneous specific binding assay device; Alfred C. Greenquist, et al., 435/7.7; 422/56, 57; 435/7.71, 7.72, 7.92, 805, 970; 436/501, 518, 531, 535, 810, 817

54. 4,659,696, Apr. 21, 1987, Pharmaceutical composition and its nasal or vaginal use; Shin-ichiro Hirai, et al., 514/15, 16, 17, 18, 19; 930/20, 21, 130

55. 4,652,441, Mar. 24, 1987, Prolonged release microcapsule and its production; Hiroaki Okada, et al., 424/497; 264/4.6; 424/DIG.15; 428/402.2; 514/2, 800, 822, 963 [IMAGE AVAILABLE]

56. 4,624,932, Nov. 25, 1986, Recognins and their chemoreciprocals; Samuel Bogoch, 436/538; 424/88; 436/530, 542, 547; 530/387, 413, 417, 814, 827

57. 4,624,931, Nov. 25, 1986, Recognins and their chemoreciprocals; Samuel Bogoch, 436/528; 424/85.8; 435/7.23, 70.3, 961; 436/530, 531, 532; 530/300, 344, 350, 387, 403

58. 4,617,307, Oct. 14, 1986, Substituted imidazo[1,5-A]pyridine

59. 4,614,712, Sep. 30, 1986, Immunoassays with luciferase labeled ligands or receptors; Thomas O. Baldwin, et al., 435/7.92, 7.93, 6, 188, 810, 964, 968, 975; 434/501, 518, 519, 533, 534, 540, 544, 546, 808

60. 4,587,102, May 6, 1986, Multi-layer analysis element utilizing specific binding reaction; Shigeru Nagatomo, et al., 422/56; 435/805; 436/810

61. 4,560,649, Dec. 24, 1985, Assaying for hLH or hCG with immobilized hormone receptors; Brij B. Saxena, et al., 435/7.21, 7.8, 7.92, 181, 188, 810, 961, 963, 964, 975; 436/501, 527, 805, 810, 817, 818; 530/313, 397, 398, 399, 812

62. 4,529,595, Jul. 16, 1985, GRF Analogs; Jean E. F. Rivier, et al., 514/12; 530/324, 334; 930/20, 21, 120

63. 4,517,290, May 14, 1985, Method for enzyme immunoassay and peptide-enzyme conjugate and antibody therefor; Susumu Iwasa, et al., 435/7.93; 424/88; 435/7.92, 188, 810, 961, 963, 967, 971, 975; 436/510, 547, 814; 530/324, 325, 326, 327, 328, 345, 387, 806; 930/10, DIG.785, DIG.811

64. 4,501,692, Feb. 26, 1985, Charge effects in enzyme immunoassays; Ian Gibbons, et al., 530/389; 424/530; 436/547; 530/390

65. 4,483,929, Nov. 20, 1984, Liposomes with glycolipid-linked antibodies; Frank C. Szoka, 436/533; 435/7.9, 8, 966; 436/512, 532, 534, 548, 800, 803, 819, 828, 829 [IMAGE AVAILABLE]

66. 4,472,498, Sep. 18, 1984, Analysis film and a method of analysis using the same; Nobuhito Masuda, et al., 435/7.7; 422/56, 57; 435/7.71, 7.72, 7.9, 805, 970; 436/500, 527, 537, 810, 815

67. 4,424,200, Jan. 3, 1984, Method for radiolabeling proteins with technetium-99m; David R. Crockford, et al., 424/1.1, 9 [IMAGE AVAILABLE]

68. 4,423,037, Dec. 27, 1983, Inhibitors of peptide hormone action; Michael Rosenblatt, et al., 514/12; 530/324, 334; 930/10, 20, 21, DIG.821

69. 4,378,428, Mar. 29, 1983, Method for carrying out non-isotopic immunoassays, labeled analytes and kits for use in such assays; Peter R. Farina, et al., 435/7.23, 7.4, 7.7, 7.8, 7.93, 188, 810, 967, 968, 971, 975; 436/500, 518, 528, 532, 536, 544; 530/345, 387, 389, 390, 391, 404, 408; 930/10, 240

70. 4,376,825, Mar. 15, 1983, Enzyme amplification compounds for assays for androgens; Kenneth E. Rubenstein, et al., 435/188

71. 4,323,546, Apr. 6, 1982, Method and composition for cancer detection in humans; David R. Crockford, et al., 436/547; 128/659; 422/61; 424/1.1, 9; 530/387, 398, 828; 534/14 [IMAGE AVAILABLE]

72. 4,287,300, Sep. 1, 1981, Charge effects in enzyme immunoassays; Ian Gibbons, et al., 435/5, 7.32, 7.9, 188, 810; 436/527, 529, 531, 546, 547, 800, 805, 806, 811, 815, 820

73. 4,282,325, Aug. 4, 1981, Enzyme bound corticosteroids; Kenneth E. Rubenstein, et al., 435/188; 930/40, 260

74. 4,240,751, Dec. 23, 1980, Method and apparatus for specific binding substances; Carl B. Linnecke, et al., 356/409; 250/227.11, 526; 356/246, 440; 422/102; 435/291, 808

75. 4,233,401, Nov. 11, 1980, Antienzyme homogeneous competitive binding assay; Robert S. Yorkey, et al., 435/7.8, 7.9, 185, 810, 963

75. 4,214,048, Jul. 22, 1980, Reagent suitable for enzyme immuno assay; Tsunehiro Kitagawa, 435/7.93, 961, 975; 436/500, 540, 544, 547, 808; 530/303, 316, 332, 398, 399, 404, 405

77. 4,200,479, Jun. 17, 1980, Label modified immunoassays; Robert F. Zuk, et al., 435/7.9, 7.72, 7.8; 436/512, 537, 808, 826

78. 4,200,802, May 20, 1980, Inhibitable enzyme amplification assay; Kenneth E. Rubenstein, et al., 435/188, 7.9, 964; 930/40, 260

79. 4,196,186, Apr. 1, 1980, Method for diagnosing malignant glial brain tumors; Samuel Bonoch, 436/503; 424/88, 573; 436/515, 530, 543; 514/21

80. 4,190,496, Feb. 26, 1980, Homogeneous enzyme assay for antibodies; Kenneth E. Rubenstein, et al., 435/7.9, 7.4, 966; 930/40, 260

81. 4,179,337, Dec. 18, 1979, Non-immunogenic polypeptides; Frank F. Davis, et al., 435/181; 424/78, 94.3, 94.4, 94.5; 435/180; 514/3; 530/303, 306, 308, 311, 313, 333, 345, 386, 397, 398, 399, 400, 405, 406, 409, 410, 816; 930/DIG.620

82. 4,150,033, Apr. 17, 1979, Reagent suitable for enzyme immuno assay; Tsunehiro Kitagawa, 548/520; 435/7.9, 961, 964; 548/544, 549

83. 4,067,774, Jan. 10, 1978, Compounds for enzyme amplification assay; Kenneth E. Rubenstein, et al., 435/188, 7.9, 189, 190, 195, 964; 930/40, 260

84. 3,975,237, Aug. 17, 1976, Compounds for enzyme amplification assay -- ecgonine analogs; Kenneth E. Rubenstein, et al., 435/188, 4, 7.9, 26, 964

85. 3,966,556, Jun. 29, 1976, Compounds for enzyme amplification assay methadone analogs; Kenneth E. Rubenstein, et al., 435/188, 7.8, 7.9, 964; 436/537, 816

86. 3,957,435, May 18, 1976, Passive hemagglutination test method and composition for use therein; Ernest Clarence Adams, et al., 436/520, 817, 818, 820, 826

87. 3,852,157, Dec. 3, 1974, COMPOUNDS FOR ENZYME AMPLIFICATION ASSAY; Kenneth E. Rubenstein, et al., 435/188, 7.8, 7.9, 18, 25, 26, 964; 436/537, 816

88. 3,839,153, Oct. 1, 1974, PROCESS FOR THE DETECTION AND DETERMINATION OF SPECIFIC BINDING PROTEINS AND THEIR CORRESPONDING BINDABLE SUBSTANCES; Antonius Hermanus Wilhelmus Maria Schuurs, et al., 435/7.93, 7.95, 188, 964, 971, 975; 436/518, 530, 531, 808, 817, 818

=> d 54 62 71 kwic

US PAT NO: 4,659,696 L8: 54 of 88

SUMMARY:

BSUM(11)

As . . . may be mentioned, for example, L-pyroglutamyl-L-histidyl-L-prolinamide (thyrotropin releasing hormone; hereinafter referred to briefly as TRH) or its salts, especially its tartrate [U.S. Pat. No. 3,957,247], and a polypeptide represented by the formula (I) ##STR1## wherein A stands for hydrogen, alkyl, aralkyl, . . .

BSUM(1A)

Examples . . . 54, 5, pp. 676-691, 1978]), oxytocin, carcitonin, parathyroid hormone, glucagon, gastrin, secretin, pancreozymin, cholecystokinin, angiotensin, human placental lactogen, human chorionic gonadotropin (HCG), enkephalin, enkephalin derivatives [U.S. Pat. No. 4,277,394; European Patent Application Publication No. 31567], endorphin, interferon (.alpha., .beta., .gamma.), urokinase, . . .

SUMMARY:

BSUM(2B)

The . . . liquid or semi-solid form. In the case of a solid form, the above components may be simply blended or be freeze - dried to provide a powdery composition, the preferred particle size in either case being about 20 to 250 microns. In the. . .

SUMMARY:

BSUM(3B)

The . . . give a solid preparation. Alternatively, the polypeptide and cyclodextrin, plus an excipient if required, are dissolved well in water and freeze - dried or spray-dried to give a dehydrated composition which is then pulverized into a solid preparation.

SUMMARY:

BSUM(54)

To . . . a wetting agent (e.g. glycerol, propylene glycol), a preservative (e.g. benzyl alcohol), a pH-adjusting agent (e.g. hydrochloric acid, acetic acid, citric acid, phosphoric acid, sodium hydroxide, potassium hydroxide, ammonia, a salt of any of these), a thickening agent (e.g. methylcellulose, carboxymethylcellulose), a stabilizer (e.g. sodium ethylenediaminetetraacetate, human serum albumin, citric acid), a dispersing agent [e.g. lecithin, Tween (polyoxyethylenesorbitan fatty acid ester, Kao-Atlas Co., Ltd. Japan), Span (higher fatty acid sorbitan. . .

SUMMARY:

BSUM(5A)

To . . . the polypeptide with a diluent such as lactose, starch or mannitol beforehand, then drying the mixed solution by way of freeze - drying or spray-drying to make a diluted powder, and molding this diluted powder into tablets. In view of the relative scarcity. . .

SUMMARY:

BSUM(59)

To . . . dissolution, there may be prepared effervescent tablets with a combination of alkali metal carbonates (e.g. sodium carbonate) or bicarbonates with citric acid or tartaric acid.

DETDESC:

DETD(46)

Heparin . . . portion of each blood sample is placed in a polyethylene pigmatube containing 0.02 ml of 3.8 w/v percent of sodium

citrate , the tube contents are stirred well and then centrifuged, and the plasma portion is subjected to prothrombin time (blood coagulation. . .

DETDESC:

DETD(60)

In . . . water are dissolved 200 mg of DN-1417, 200 mg of mannitol and 200 mg of .beta.-cyclodextrin and the solution is freeze - dried . The dry product is then pulverized to give a powder about 20 to 250 microns in diameter. A 30 mg. . .

DETDESC:

DETD(78)

In . . . there are dissolved and dispersed 20 g of lactose and 20,000 units (about 800 mg) of porcine insulin, followed by lyophilization . Thereafter, the lyophilizate is ground and stirred well. To a 10.4 g portion of the lyophilizate, there is added a. . .

DETDESC:

DETD(84)

.alpha.-Cyclodextrin (0.5 g), thyroid hormone-releasing hormone (TRH) tartrate (141.4 mg; 100 mg as TRH) and glycerin (180 ml) are dissolved in distilled water to make 10 ml. A. . .

DETDESC:

DETD(86)

.alpha.-Cyclodextrin . . . 10 ml of distilled water. Glass bottles are each filled with 2 ml of the solution and the contents are lyophilized . Immediately before use, the lyophilizate is dissolved in 2 ml of a diluent of distilled water and the bottle is. . .

DETDESC:

DETD(88)

Witepsol . . . 500 mg of .alpha.- or .beta.-cyclodextrin is added thereto. The mixture is stirred with warming. Then, 183.6 mg of DN-1417 citrate (corresponding to 120 mg of DN-1417) is added. The resultant mixture is stirred well and poured into a 1 g. . .

DETDESC:

DETD(90)

In . . . 25 w/w percent of PEG 4000. The base is melted with warming at 50.degree.-60.degree. C. .alpha.- or .beta.-cyclodextrin and DN-1417 citrate are added thereto and the mixture is treated in the manner in Example 16 to give ten 1 g rectal. . .

DETDESC:

DETD(92)

To . . . mixture is stirred to prepare a dispersion. Thereto is added 28 ml of solution A containing 1.414 g of TRH tartrate (corresponding to 1 g of TRH) and 5 g of .alpha.-cyclodextrin dissolved therein. The resultant mixture is cooled to 4.degree.. . .

DETDESC:

DETD(94)

To . . . mixture is stirred to prepare a dispersion. Thereto is added 38 ml of solution A containing 1.414 g of TRH tartrate (corresponding to 1 g of TRH) and 5 g of .alpha.-cyclodextrin dissolved therein. The resultant mixture is cooled to 4.degree.. . . .

CLAIMS:

CLMS(9)

9. . . . stimulating hormone, vasopressin, vasopressin derivatives, oxytocin, carcitonin, parathyroid hormone, glucagon, gastrin, secretin, pancreozymin, cholecystokinin, angiotensin, human placental lactogen, human chorionic gonadotropin , enkephalin, enkephalin derivatives, endorphin, interferon (.alpha., .beta., .gamma.), urokinase, kallikrein, thymopoietin, thymosin, motilin, dynorphin, bombesin, neurotensin, caerulein, bradykinin, substance P,. . .

CLAIMS:

CLMS(22)

22. . . . stimulating hormone, vasopressin, vasopressin derivatives, oxytocin, carcitonin, parathyroid hormone, glucagon, gastrin, secretin, pancreozymin, cholecrystokinin, angiotensin, human placental lactogen, human chorionic gonadotropin , enkephalin, enkephalin derivatives, endorphin, interferon (.alpha., .beta., .gamma.), urokinase, kallikrein, thymopoietin, thymosin, motilin, dynorphin, bombesin, neurotensin, caerulein, bradykinin, substance P,. . .

US PAT NO: 4,529,595 L8: 62 of 88

SUMMARY:

BSUM(3)

Physiologists . . . hypothalamic releasing factor has been characterized for the pituitary hormones thyrotropin and prolactin (i.e. the tripeptide TRF), for the pituitary gonadotropins , luteinizing hormone and follicle stimulating hormone (i.e. the decapeptide LRF, LH-RH or GnRH) and for the pituitary hormones .beta.-endorphin and. . .

SUMMARY:

BSUM(10)

The hpGRF analogs having one of the named substituents for Met in the 27-position exhibit substantially greater stability , particularly when exposed to oxidizing conditions; moreover, if the substituent is a D-isomer, enzyme resistance may be enhanced. They remain. . .

DETDESC:

DETD(11)

The . . . independently checked for purity, is achieved using a gradient of CH.sub.3 CN in 0.1% TFA. The center cut is then lyophilized to yield the desired peptide, the purity of which is greater than 98%.

DETDESC:

DETD(64)

Such . . . as salts for purposes of this application). Illustrative of such acid addition salts are hydrochloride, hydrobromide, sulphate, phosphate, maleate, acetate, citrate, benzoate, succinate, malate, ascorbate, tartrate and the like. If the active ingredient is to be orally administered in tablet form, the tablet may contain a. . .

US PAT NO: 4,323,546 [IMAGE AVAILABLE] L8: 71 of 88

ABSTRACT:
Anti human chorionic gonadotropin (anti-hCG) and/or anti human chorionic gonadotropin - beta subunit (anti-hCG-.beta.) labeled with Technetium-99M are/is administered to a human. The biodistribution of the labeled composition is monitored in order to determine whether the labeled composition accumulates at cancer sites, e.g. tumors that produce human chorionic gonadotropin (hCG), human chorionic gonadotropin -like material, and a compound similar to and/or identical to the beta-chain of chorionic gonadotropin, or mixtures thereof which would bind specifically to anti-hCG and/or anti-hCG-.beta..

SUMMARY:

BSUM(2)

This . . . will accumulate at cells producing hCG, hCG-like material, and a compound similar to and/or identical to the beta-chain of chorionic gonadotropin, or mixtures thereof.

SUMMARY:

BSUM(3)

The . . . to form diagnostic agents. It has also been proposed to tag the antibody of the beta chain of human chorionic gonadotropin with peroxidase (McManus et al, Cancer Research, 36, pp. 2367-3481, September, 1976) in order to localize the antigen in malignant. . .

SUMMARY:

BSUM(4)

Recently, it has been found that neoplastic tissues produce chorionic gonadotropin, chorionic gonadotropin -like material, and a compound similar to and/or identical to the .beta.-chain of chorionic gonadotropin (hCG-.beta. subunit) or mixtures thereof, specifically to the degree where it is considered more cancer specific than either carcinoembryonic antigen (CEA) or alphafetoprotein (AFP). The positive identification of chorionic gonadotropin in a heterogenous group of cancer cells and its absence in non-cancer cells in tissue culture has suggested that:

SUMMARY:

BSUM(8)
It is also believed that chorionic gonadotropin is one of the factors involved in maternal immunosuppression. In support of this belief, it has been shown that chorionic gonadotropin has been shown to block maternal lymphocyte cytotoxicity, maternal lymphocyte mitosis and to inhibit phytohemagglutin-induced and mixed lymphocyte blast transformation.

DETDESC:

DETD(2)

Human chorionic gonadotropin (hCG) is a molecule believed to have a

molecular weight ranging from about 35,000 and 38,000. HCG is found in.

DETDESC:

DETD(7)

A . . . solution of SnCl.sub.2 which is a reducing agent for pertechnetate. The buffered solution can comprise sodium and or potassium phthalate, tartrate , gentisate, acetate, borate or mixtures thereof having a pH of between 4.5 and 8.0, preferably about 5.5. Tartrate is utilized to maintain the appropriate concentration of stannous ion in solution to effect the desired solution pH. The SnCl.sub.2. . . hours. If desired, this solution can be heated moderately to reduce the incubation time. The solution then can be either freeze - dried and subsequently reconstituted for admixture with pertechnetate or can be admixed direc

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s gonadotropin?
L1          1023 GONADOTROPIN?

=> s l1 and recombinant
            3583 RECOMBINANT
L2            93 L1 AND RECOMBINANT

=> s l2 and (citric or isocitric or tartaric or aspartic or glutamic)
           31843 CITRIC
             217 ISOCITRIC
           18845 TARTARIC
            5401 ASPARTIC
            6839 GLUTAMIC
L3            30 L2 AND (CITRIC OR ISOCITRIC OR TARTARIC OR ASPARTIC OR GLUT
AMI
                 C)

=> s ?reducing sugar? or sucrose or trehalose
          309220 ?REDUCING
           40329 SUGAR?
            1694 ?REDUCING SUGAR?
                   (?REDUCING(W)SUGAR?)
           25295 SUCROSE
            1115 TREHALOSE
L4         26480 ?REDUCING SUGAR? OR SUCROSE OR TREHALOSE

=> s l3 and l4
L5            11 L3 AND L4

=> d 1-11

1.  5,135,523, Aug. 4, 1992, Delivery system for administering agent to
ruminants and swine; Judy A. Magruder, et al., 604/892.1; 424/438, 473;
604/890.1 [IMAGE AVAILABLE]

2.  5,110,597, May 5, 1992, Multi-unit delivery system; Patrick S. L.
Wong, et al., 424/438, 473 [IMAGE AVAILABLE]

3.  5,110,596, May 5, 1992, Delivery system comprising means for
delivering agent to livestock; Judy A. Magruder, et al., 424/438, 473
[IMAGE AVAILABLE]

4.  5,100,788, Mar. 31, 1992, Method of producing and isolating
IGG-binding protein a fusion peptides and a vector therefor; Sven
Lofdahl, et al., 435/69.7, 71.2, 91, 172.3, 252.3, 252.31, 252.33, 320.1
[IMAGE AVAILABLE]

5.  5,059,423, Oct. 22, 1991, Delivery system comprising biocompatible
beneficial agent formulation; Judy A. Magruder, et al., 424/438, 422,
423, 426, 473 [IMAGE AVAILABLE]

6.  5,057,318, Oct. 15, 1991, Delivery system for beneficial agent over a
broad range of rates; Judy A. Magruder, et al., 424/438, 423, 426, 472,
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7. 5,037,420, Aug. 6, 1991, Delivery system comprising two sections for delivering somatotropin; Judy A. Magruder, et al., 604/892.1 [IMAGE AVAILABLE]

8. 5,034,229, Jul. 23, 1991, Dispenser for increasing feed conversion of hog; Judy A. Magruder, et al., 424/422, 423, 426, 473, 484, 486 [IMAGE AVAILABLE]

9. 5,023,088, Jun. 11, 1991, Multi-unit delivery system; Patrick S. L. Wong, et al., 424/473, 405, 408, 438, 472; 604/892.1 [IMAGE AVAILABLE]

10. 4,957,494, Sep. 18, 1990, Multi-layer delivery system; Patrick S. L. Wong, et al., 604/892.1, 131, 891.1 [IMAGE AVAILABLE]

11. 4,766,069, Aug. 23, 1988, Recombinant DNA which codes for interleukin-1 B; Philip E. Auron, et al., 435/69.52, 91, 172.1, 172.3, 240.1, 240.2, 243, 252.3, 252.33, 255, 256, 320.1; 530/351; 536/27; 930/141; 935/11, 27, 66, 72, 73

=>

s l3 and (lyophiliz? or freeze dried or freeze drying)
- 11301 LYOPHILIZ?
- 24197 FREEZE
- 212130 DRIED
- 6722 FREEZE DRIED
  - (FREEZE(W)DRIED)
- 24197 FREEZE
- 149638 DRYING
- 5413 FREEZE DRYING
  - (FREEZE(W)DRYING)

L6 12 L3 AND (LYOPHILIZ? OR FREEZE DRIED OR FREEZE DRYING)

=> d 1-12

1. 5,112,804, May 12, 1992, Pharmaceutical composition and method of intranasal administration; Hanna R. Kowarski, 514/3; 424/434; 514/4, 12, 13, 14, 15, 947, 970 [IMAGE AVAILABLE]

2. 5,106,762, Apr. 21, 1992, Ligand-label conjugates which contain polyoxoanions of sulfur or phosphorus; Reinhard Bredehorst, et al., 436/546, 501, 543, 544, 547; 530/303, 324, 325, 326, 327, 328, 329, 330 [IMAGE AVAILABLE]

3. 5,102,868, Apr. 7, 1992, Method for inhibiting follicular maturation; Teresa K. Woodruff, et al., 514/8; 424/559; 514/12, 21 [IMAGE AVAILABLE]

4. 5,100,788, Mar. 31, 1992, Method of producing and isolating IGG-binding protein a fusion peptides and a vector therefor; Sven Lofdahl, et al., 435/69.7, 71.2, 91, 172.3, 252.3, 252.31, 252.33, 320.1 [IMAGE AVAILABLE]

[redacted]089,396, Feb. 18, 1992, Nucleic acid encoding .beta. chain [redacted]ains of inhibin and method for synthesizing polypeptides using such [redacted]ic acid; Anthony J. Mason, et al., 435/69.1, 69.4, 240.2, 252.3, [redacted]; 536/27; 935/11 [IMAGE AVAILABLE]

6. 5,075,224, Dec. 24, 1991, Prepro-LHRH C-terminal peptide DNA; Peter H. Seeburg, et al., 435/69.4, 172.3, 240.1, 240.2, 252.33, 320.1; 536/27; 935/13, 47, 48, 69, 72, 73 [IMAGE AVAILABLE]

7. 5,037,805, Aug. 6, 1991, Methods of contraception; Nicholas C. Ling, 514/8; 424/85.8; 514/21; 530/395 [IMAGE AVAILABLE]

8. 5,015,729, May 14, 1991, Ovine inhibin; Joachim Spiess, et al., 530/350, 387.9, 389.2, 397, 398 [IMAGE AVAILABLE]

9. 4,914,189, Apr. 3, 1990, Synthetic GHRH analogs; Andrew V. Schally, et al., 530/324 [IMAGE AVAILABLE]

10. 4,798,885, Jan. 17, 1989, Compositions of hormonally active human and porcine inhibin containing an .alpha. chain and 62 chain; Anthony J. Mason, et al., 530/350; 930/10, 260, DIG.530, DIG.821

11. 4,777,127, Oct. 11, 1988, Human retrovirus-related products and methods of diagnosing and treating conditions associated with said retrovirus; Jukka Suni, et al., 435/5; 436/518, 531, 813, 822; 530/300, 327, 328, 387.9, 388.35, 388.85, 388.9, 389.4, 389.7, 389.8, 820, 826, 827, 828; 930/221, DIG.802

12. 4,687,732, Aug. 18, 1987, Visualization polymers and their application to diagnostic medicine; David C. Ward, et al., 435/6, 7.4, 7.5, 7.72, 7.9, 14, 21, 25, 28, 188, 810, 968, 975; 436/501, 504, 537, 545, 546, 800, 801, 804, 808, 827

=>

d 13 1-30

1. 5,135,523, Aug. 4, 1992, Delivery system for administering agent to ruminants and swine; Judy A. Magruder, et al., 604/892.1; 424/438, 473; 604/890.1 [IMAGE AVAILABLE]

2. 5,112,804, May 12, 1992, Pharmaceutical composition and method of intranasal administration; Hanna R. Kowarski, 514/3; 424/434; 514/4, 12, 13, 14, 15, 947, 970 [IMAGE AVAILABLE]

3. 5,110,597, May 5, 1992, Multi-unit delivery system; Patrick S. L. Wong, et al., 424/438, 473 [IMAGE AVAILABLE]

4. 5,110,596, May 5, 1992, Delivery system comprising means for delivering agent to livestock; Judy A. Magruder, et al., 424/438, 473 [IMAGE AVAILABLE]

5. 5,106,762, Apr. 21, 1992, Ligand-label conjugates which contain polyoxoanions of sultur or phosphorus; Reinhard Bredehorst, et al., 436/546, 501, 543, 544, 547; 530/303, 324, 325, 326, 327, 328, 329, 330

6. 5,103,836, Apr. 14, 1992, Oral collection device and kit for immunoassay; Andrew S. Goldstein, et al., 128/760; 206/569 [IMAGE AVAILABLE]

7. 5,102,868, Apr. 7, 1992, Method for inhibiting follicular maturation; Teresa K. Woodruff, et al., 514/8; 424/559; 514/12, 21 [IMAGE AVAILABLE]

8. 5,100,788, Mar. 31, 1992, Method of producing and isolating IGG-binding protein a fusion peptides and a vector therefor; Sven Lofdahl, et al., 435/69.7, 71.2, 91, 172.3, 252.3, 252.31, 252.33, 320.1 [IMAGE AVAILABLE]

9. 5,089,396, Feb. 18, 1992, Nucleic acid encoding .beta. chain prodomains of inhibin and method for synthesizing polypeptides using such nucleic acid; Anthony J. Mason, et al., 435/69.1, 69.4, 240.2, 252.3, 320.1; 536/27; 935/11 [IMAGE AVAILABLE]

10. 5,077,195, Dec. 31, 1991, Polypeptides complementary to peptides or proteins having an amino acid sequence or nucleotide coding sequence at least partially known and methods of design therefor; J. Edwin Blalock, et al., 435/6, 5, 172.3, 803; 436/501 [IMAGE AVAILABLE]

11. 5,075,224, Dec. 24, 1991, Prepro-LHRH C-terminal peptide DNA; Peter H. Seeburg, et al., 435/69.4, 172.3, 240.1, 240.2, 252.33, 320.1; 536/27; 935/13, 47, 48, 69, 72, 73 [IMAGE AVAILABLE]

12. 5,059,423, Oct. 22, 1991, Delivery system comprising biocompatible beneficial agent formulation; Judy A. Magruder, et al., 424/438, 422, 423, 426, 473 [IMAGE AVAILABLE]

13. 5,057,318, Oct. 15, 1991, Delivery system for beneficial agent over a broad range of rates; Judy A. Magruder, et al., 424/438, 423, 426, 472, 473 [IMAGE AVAILABLE]

14. 5,037,805, Aug. 6, 1991, Methods of contraception; Nicholas C. Ling, 514/8; 424/85.8; 514/21; 530/395 [IMAGE AVAILABLE]

15. 5,037,420, Aug. 6, 1991, Delivery system comprising two sections for delivering somatotropin; Judy A. Magruder, et al., 604/892.1 [IMAGE AVAILABLE]

16. 5,034,229, Jul. 23, 1991, Dispenser for increasing feed conversion of hog; Judy A. Magruder, et al., 424/422, 423, 426, 473, 484, 486 [IMAGE AVAILABLE]

17. 5,023,088, Jun. 11, 1991, Multi-unit delivery system; Patrick S. L. Wong, et al., 424/473, 405, 408, 438, 472; 604/892.1 [IMAGE AVAILABLE]

18. 5,015,729, May 14, 1991, Ovine inhibin; Joachim Spiess, et al., 530/350, 387.9, 389.2, 397, 398 [IMAGE AVAILABLE]

19. 4,959,217, Sep. 25, 1990, Delayed/sustained release of macromolecules; Lynda M. Sanders, et al., 424/473, 425, 427, 433, 436, 486, 487 [IMAGE AVAILABLE]

20. 4,957,494, Sep. 18, 1990, Multi-layer delivery system; Patrick S. L. Wong, et al., 604/892.1, 131, 891.1 [IMAGE AVAILABLE]
KMM5&$M4914,189, Apr. 3, 1990, Synthetic GHRH analogs; Andrew V. Schally, et al., 530/324 [IMAGE AVAILABLE]

22. 4,864,019, Sep. 5, 1989, Antibodies to inhibin and conjugates produced therefrom; Wylie W. Vale, et al., 424/85.8, 88; 435/7.92; 525/54.1; 530/387.9, 389.2 [IMAGE AVAILABLE]

proteins having an amino acid sequence or nucleotide coding sequence at least partially known; J. Edwin Blalock, et al., 435/69.1, 6, 68.1, 69.4, 240.2, 803, 948; 436/501; 930/10, 70, 80, 120, 130, 141; 935/78

24. 4,803,156, Feb. 7, 1989, Peptide-beta-lactamase conjugates for enzyme-linked immunoassays; Alexander R. Neurath, et al., 435/5, 7.92, 18, 19; 436/820, 828; 930/142, 200, 221, 222, 223, 260, 310, DIG.820

25. 4,798,885, Jan. 17, 1989, Compositions of hormonally active human and porcine inhibin containing an .alpha. chain and 62 chain; Anthony J. Mason, et al., 530/350; 930/10, 260, DIG.530, DIG.821

26. 4,777,127, Oct. 11, 1988, Human retrovirus-related products and methods of diagnosing and treating conditions associated with said retrovirus; Jukka Suni, et al., 435/5; 436/518, 531, 813, 822; 530/300, 327, 328, 387.9, 388.35, 388.85, 388.9, 389.4, 389.7, 389.8, 820, 826, 827, 828; 930/221, DIG.802

27. 4,766,069, Aug. 23, 1988, Recombinant DNA which codes for interleukin-1 B; Philip E. Auron, et al., 435/69.52, 91, 172.1, 172.3, 240.1, 240.2, 243, 252.3, 252.33, 255, 256, 320.1; 530/351; 536/27; 930/141; 935/11, 27, 66, 72, 73

28. 4,687,732, Aug. 18, 1987, Visualization polymers and their application to diagnostic medicine; David C. Ward, et al., 435/6, 7.4, 7.5, 7.72, 7.9, 14, 21, 25, 28, 188, 810, 968, 975; 436/501, 504, 537, 545, 546, 800, 801, 804, 808, 827

29. 4,578,217, Mar. 25, 1986, Synthetic antigenic peptide derived from hepatitis B surface antigen; John Vnek, et al., 530/327, 329, 806; 930/223

30. 4,575,495, Mar. 11, 1986, Synthetic antigenic peptide derived from Hepatitis B surface antigen; John Vnek, et al., 514/16; 930/223, DIG.802

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U.S. Patent & Trademark Office LOGOFF AT 09:06:29 ON 23 OCT 92

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s gonadotropin?
L1          1083 GONADOTROPIN?

=> s l1 and (citric or tartaric or aspartic or isocitric or glutamic)
           33081 CITRIC
           19567 TARTARIC
            5756 ASPARTIC
             224 ISOCITRIC
            7274 GLUTAMIC
L2           316 L1 AND (CITRIC OR TARTARIC OR ASPARTIC OR ISOCITRIC OR GLUT
AMI
                 C)

=> s l2 and stabili?
          314947 STABILI?
L3           158 L2 AND STABILI?

=> s l3 and (sucrose or trehalose)
           26367 SUCROSE
            1179 TREHALOSE
L4             46 L3 AND (SUCROSE OR TREHALOSE)

=>
d 1-46

1.  5,196,564, Mar. 23, 1993, Physiologically active substance THN-9o1,
its derivatives, their production and use; Tsuneo Kanamaru, et al..
560/52; 435/183; 560/35, 54 [IMAGE AVAILABLE]

2.  5,174,999, Dec. 29, 1992, Delivery system comprising fluid inqress
and drug egress; Judy A. Magruder, et al., 424/424, 422, 426, 473 [IMAGE
AVAILABLE]

3.  5,153,000, Oct. 6, 1992, Phosphate, liposome comprising the phosphate
as membrane constituent, and cosmetic and liposome preparation comprising
the liposome; Yoshiko Chikawa, et al., 424/450; 252/4.1; 424/401, 417;
558/160, 163, 164 [IMAGE AVAILABLE]

4.  5,135,523, Aug. 4, 1992, Delivery system for administering agent to
ruminants and swine; Judy A. Magruder, et al., 604/892.1; 424/438, 473;
604/890.1 [IMAGE AVAILABLE]

5.  5,112,845, May 12, 1992, Alpha-heterocycle substituted tolunitriles;
Robert M. Bowman, et al., 514/399, 341 [IMAGE AVAILABLE]
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6. 5,116,357, May 5, 1992, Multi-unit delivery system, Patrick S. L. Wong, et al., 424/438, 473 [IMAGE AVAILABLE]

7. 5,110,596, May 5, 1992, Delivery system comprising means for delivering agent to livestock; Judy A. Magruder, et al., 424/438. 473 [IMAGE AVAILABLE]

8. 5,071,861, Dec. 10, 1991, Alpha-heterocycle substituted tolunitriles; Robert M. Bowman, et al., 514/332, 278, 357; 546/15, 264, 330 [IMAGE AVAILABLE]

9. 5,061,492, Oct. 29, 1991, Prolonged release microcapsule of a water-soluble drug; Hiroaki Okada, et al., 424/423, 426, 497, 499; 428/402.2; 514/963 [IMAGE AVAILABLE]

10. 5,059,423, Oct. 22, 1991, Delivery system comprising biocompatible beneficial agent formulation; Judy A. Magruder, et al., 424/438, 422, 423, 426, 473 [IMAGE AVAILABLE]

11. 5,057,318, Oct. 15, 1991, Delivery system for beneficial agent over a broad range of rates; Judy A. Magruder, et al., 424/438, 423, 426, 472, 473 [IMAGE AVAILABLE]

12. 5,037,420, Aug. 6, 1991, Delivery system comprising two sections for delivering somatotropin; Judy A. Magruder, et al., 604/892.1 [IMAGE AVAILABLE]

13. 5,034,229, Jul. 23, 1991, Dispenser for increasing feed conversion of hog; Judy A. Magruder, et al., 424/422, 423, 426, 473, 484, 486 [IMAGE AVAILABLE]

14. 5,023,088, Jun. 11, 1991, Multi-unit delivery system; Patrick S. L. Wong, et al., 424/473, 405, 408, 438, 472; 604/892.1 [IMAGE AVAILABLE]

15. 5,013,757, May 7, 1991, Physiologically active substance Tan-931, its derivatives, their production and use; Tsuneo Kanamaru, et al., 514/568; 544/3, 8, 174, 176, 391; 546/226; 548/127, 128, 214, 578; 560/56; 562/440, 441, 460; 564/167, 169 [IMAGE AVAILABLE]

16. 4,978,672, Dec. 18, 1990, Alpha-heterocycle substituted tolunitriles; Robert M. Bowman, et al., 514/338, 333, 340; 546/256, 276; 548/262.2 [IMAGE AVAILABLE]

17. 4,966,888, Oct. 30, 1990, hCG-hLH receptor and hCG-hLH receptor-hCG complex as antigens, antibodies thereto and contraceptive vaccine; Brij B. Saxena, et al., 514/2; 424/88; 435/70.1, 70.3; 514/8, 12; 530/330, 398, 399 [IMAGE AVAILABLE]

18. 4,966,856, Oct. 30, 1990, Analytical element and the analytical method using the element; Tsukasa Ito, et al., 436/170; 422/56, 57, 58; 435/4, 7.8, 7.93, 28, 805, 970; 436/172, 804, 805 [IMAGE AVAILABLE]

19. 4,963,581, Oct. 16, 1990, Naphthopyran derivatives and use thereof; Tsuneo Kanamaru, et al., 514/455; 549/280 [IMAGE AVAILABLE]

20. 4,957,494, Sep. 18, 1990, Multi-layer delivery system; Patrick S. L. Wong, et al., 604/892.1, 131, 891.1 [IMAGE AVAILABLE]

21. 4,937,250, Jun. 26, 1990, Alpha-heterocycle substituted tolunitriles; Robert M. Bowman, et al., 514/341, 399; 546/278; 548/345.1, 346.1 [IMAGE AVAILABLE]

22. 4,935,543, Jun. 19, 1990, Physiologically active substance tan-931, its derivatives, their production and use; Tsuneo Kanamaru, et al., 564/169; 544/3, 8, 174, 176, 391; 546/226; 548/127, 128, 214, 578; 560/56; 562/440, 441, 460; 564/167 [IMAGE AVAILABLE]

23. 4,931,385, Jun. 5, 1990. Enzyme immunoassays and immunologic reagents; Elliott Block, et al., 435/7.94, 28. 188. 805. 810. 975; 436/518, 808, 810, 814, 818, 826 [IMAGE AVAILABLE]

24. 4,917,893, Apr. 17, 1990, Prolonged release microcapsules; Hiroaki Okada, et al., 424/423, 433, 497, 499, 500; 428/402.2; 514/2, 800, 822, 963 [IMAGE AVAILABLE]

25. 4,880,914, Nov. 14, 1989, Assay for qualitatively and/or quantitatively measuring hLH or hCG in body fluids and reagents therefor; Brij B. Saxena, et al., 530/395; 424/88; 514/8; 530/397, 398, 412, 413

26. 4,868,106, Sep. 19, 1989, Analytical element and method for determining a component in a test sample; Tsukasa Ito, et al., 435/7.7; 422/56, 57; 435/7.5, 7.71, 7.72, 7.8, 7.92, 7.94, 805, 968; 436/501, 518, 524, 527, 528, 529, 530, 531, 800, 810, 827, 828

27. 4,855,285, Aug. 8, 1989, Antigenic modification of polypeptides; Vernon C. Stevens, 514/12, 13; 930/20, 40, 110, 220

28. 4,760,030, Jul. 26, 1988, Quantitative opaque particle agglutination assay; Paulette Peterson, et al., 436/509, 528, 534, 805, 808, 909

29. 4,713,366, Dec. 15, 1987, Antigenic modification of polypeptides; Vernon C. Stevens, 514/13; 530/326, 403; 930/21, 110, 290

30. 4,711,782, Dec. 8, 1987, Prolonged release microcapsules and their production; Hiroaki Okada, et al., 424/455; 264/4.6; 424/457, 497; 428/402.2; 514/963 [IMAGE AVAILABLE]

31. 4,670,419, Jun. 2, 1987, Pharmaceutical composition and its rectal use; Yoshiaki Uda, et al., 514/16, 17, 18, 19. 800, 805. 807, 809; 930/20, 21, 130

32. 4,659,696, Apr. 21, 1987, Pharmaceutical composition and its nasal or vaginal use; Shin-ichiro Hirai, et al., 514/15, 16, 17, 18. 19; 930/20, 21, 130

33. 4,652,441, Mar. 24, 1987, Prolonged release microcapsule and its production; Hiroaki Okada, et al., 424/497; 264/4.6; 424/DIG.15; 428/402.2; 514/2, 800, 822, 963 [IMAGE AVAILABLE]

34. 4,560,649, Dec. 24, 1985, Assaying for hLH or hCG with immobilized hormone receptors; Brij B. Saxena, et al., 435/7.21, 7.8, 7.92, 181, 188, 810, 961, 963, 964, 975; 436/501, 527, 805, 810, 817, 818; 530/313, 397, 398, 399, 812

35. 4,517,290, May 14, 1985, Method for enzyme immunoassay and peptide-enzyme conjugate and antibody therefor; Susumu Iwasa, et al., 435/7.93; 424/88; 435/7.92, 188, 810, 961, 963, 967, 971, 975; 436/510, 547, 814; 530/324, 325, 326, 327, 328, 345, 387.9, 389.2, 806; 930/10. DIG.785, DIG.811

36. 4,423,037, Dec. 27, 1983, Inhibitors of peptide hormone action; Michael Rosenblatt, et al., 514/12; 530/324, 334; 930/10, 20, 21. DIG.821

37. 4,376,825, Mar. 15, 1983, Enzyme amplification compounds for assays for androgens; Kenneth E. Rubenstein, et al., 435/188

38. 4,282,325, Aug. 4, 1981, Enzyme bound corticosteroids; Kenneth E. Rubenstein, et al., 435/188; 930/40, 260

39. 4,203,802, May 20, 1980, Inhibitable enzyme amplification assay; Kenneth E. Rubenstein, et al., 435/188, 7.9. 964; 930/40. 260

40. 4,190,496, Feb. 26, 1980, Homogeneous enzyme assay for antibodies; Kenneth E. Rubenstein, et al., 435/7.9, 7.4, 966; 930/40, 260

41. 4,067,774, Jan. 10, 1978, Compounds for enzyme amplification assay; Kenneth E. Rubenstein, et al., 435/188, 7.9, 189, 190, 195, 964; 930/40, 260

42. 3,975,237, Aug. 17, 1976, Compounds for enzyme amplification assay -- ecgonine analogs; Kenneth E. Rubenstein, et al., 435/188, 4, 7.9, 26, 964

43. 3,966,556, Jun. 29, 1976, Compounds for enzyme amplification assay methadone analogs; Kenneth E. Rubenstein, et al., 435/188, 7.8, 7.9, 964; 436/537, 816

44. 3,957,435, May 18, 1976, Passive hemagglutination test method and composition for use therein; Ernest Clarence Adams, et al., 436/526, 817, 818, 820, 826

45. 3,934,015, Jan. 20, 1976, Oral male antifertility method and compositions; Alfred Boris, 514/317; 424/DIG.1; 514/235.5, 239.5, 316

46. 3,852,157, Dec. 3, 1974, COMPOUNDS FOR ENZYME AMPLIFICATION ASSAY; Kenneth E. Rubenstein, et al., 435/188, 7.8, 7.9, 18, 25, 26, 964; 436/537, 816

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